NUCLEIC ACID SEQUENCE

GTCGACCCACGCGTCCGGCCCTGGAGAAAGGAAGAAACTTATAATAAATG
GGAAATTATAAATCTAGACCAACCCAAACTTGTACTGATGAATGGAAGAA
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AGACCCCTCCACCTAGCATCTGCAAAAGGATTCTTGAATATTGCAAAACT
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Fig. 1A

CCCACTATTAGCAGGCTTTGGATTTGTGCCTAAGGAATAATATGCAAAAG
AACCAAGACAGAATGTATATGAAGAATTGTTTTTAATTTTGTAAATTAAA
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GCTATGGGTTTATTTCTTAGAACATTGTTCATTTTCTTTTCTCATTATGT
TACTTCTAGTGTTCACCTCTGTGATTAAAGATTCTTTGGTGAAATAGAAA
AAAAAAAAAAAAAAAGGGCGGCCGC

AMINO ACID SEQUENCE

MGNYKSRPTQTCTDEWKKKVSESYVITIERLEDDLQIKEKELTELRNIFGSDEAFSKVNL
NYRTENGLSLLHLCCICGGKKSHIRTLMLKGLRPSRLTRNGFTALHLAVYKDNAELITSL
LHSGADIQQVGYGGLTALHIATIAGHLEAADVLLQHGANVNIQDAVFFTPLHIAAYYGHE
QVTRLLLKFGADVNVSGEVGDRPLHLASAKGFLNIAKLLMEEGSKADVNAQDVEDHVPLH
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DNGADMNLVACDPSRSSGEKDEQTCLMWAYEKGHDAIVTLLKHYKRPQDELPCNEYSQPG
GDGSYVSVPSPLGKIKSMTKEKADILLLRAGLPSHFHLQLSEIEFHEIIGSGSFGKVYKG
RCRNKIVAIKRYRANTYCSKSDVDMFCREVSILCQLNHPCVIQFVGACLNDPSQFAIVTQ
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HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFSYALCLWEILT
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ECLCNIELMSPASSNSSGSLSPSSSSDCLVNRGGPGRSHVAALRSRFELEYALNARSYAA
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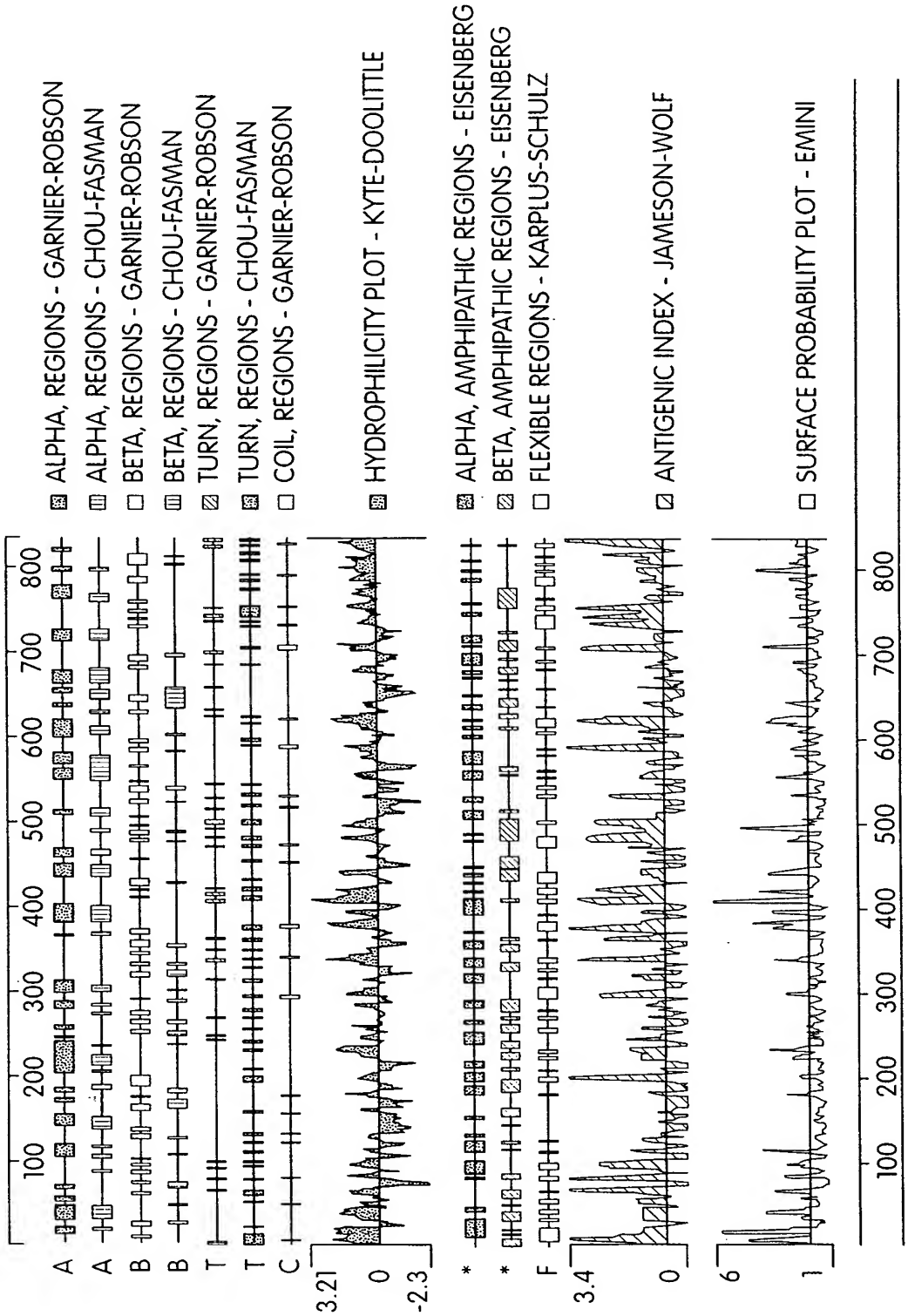
Fig. 1B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ALPHA, REGIONS - CHOU-FASMAN
BETA, REGIONS - GARNIER-ROBSON
BETA, REGIONS - CHOU-FASMAN
TURN, REGIONS - GARNIER-ROBSON
TURN, REGIONS - CHOU-FASMAN
COIL, REGIONS - GARNIER-ROBSON
HYDROPHILICITY PLOT - KYTE-DOOLITTLE
ALPHA, AMPHIPATHIC REGIONS - EISENBERG
BETA, AMPHIPATHIC REGIONS - EISENBERG
FLEXIBLE REGIONS - KARPLUS-SCHULZ
ANTIGENIC INDEX - JAMESON-WOLF
SURFACE PROBABILITY PLOT - EMINI
100
200
300
400
500
600
700
800
3.21
0
-2.3
3.4
0
6
1

Fig. 2

```
   MEEI----------EW-KT-S---------  Majority
             10        20        30
1  MGNYKSRPTQTCTDEWKKKVSESYVITIER  CARP2/prot
1  MEKK---------SEE---------------  A.thaliana kinase2
1  MSG-----------------------LC--  A.thaliana3
1  MSCSSSSGSEGEEEGFDA------------  Arabidopsis thaliana
1  MRTF---------SDELKKKISEGYSVVRSR  c.elegans kinase
1  ----------------------------  D.discoideum (A35670)
1  GTET---------T-----RMEED-QISC-S  D.Discoideum (U01064)
1  MEEEEG----AVAKEWGTTPAGPVWTAVFD  H.sapiens (Z48615)
1  MEEEEG----AVAKEWGTTPAGPVWTAVFD  Homo sapiens (Z48615)
1  MEHIQG---------AW-KTISNGF------  Human raf1(W13107)
1  MEHIQG---------AW-KTISNGF------  Human Raflkinase(R98215)
1  MGED---------GNSWIRRTNFS-HTVCHR  Soybean kinase(M67449)

   ----------L-----------------  Majority
             40        50        60
31 LEDDLQIK-------------EKELTELRN  CARP2/prot
8  ----------------------------  A.thaliana kinase2
6  FN-----PFRL-----------------  A.thaliana3
19 ----------YRKGGYHAVRIGDPFSGGRY  Arabidopsis thaliana
23 LSDDVRSRSNLGWVDVQIAAFEKSLEDFKQ  c.elegans kinase
1  ----------------------------  D.discoideum (A35670)
16 ID-----VYAYAFV------------LWE  D.Discoideum (U01064)
27 YEAAGDEELTLRRGD-RVQVLSQD-----C  H.sapiens (Z48615)
27 YEAAGDEELTLRRGD-RVQVLSQD-----C  Homo sapiens (Z48615)
16 ----------------GFKDAVFDGS------  Human raf1(W13107)
16 ----------------GFKDAVFDGS------  Human Raflkinase(R98215)
22 LD-----PARLGSI-------------PIS  Soybean kinase(M67449)

   ----------------------------  Majority
             70        80        90
48 IFGSDEAFSKVNLNYRTENGLSLLHLCCIC  CARP2/prot
8  ----------------------------  A.thaliana kinase2
12 ---------RW-----------------  A.thaliana3
39 IAQRKLGW-----------------------  Arabidopsis thaliana
53 HMCPENA------ELKSTQLLSLFHIICA-  c.elegans kinase
1  ----------------------------  D.discoideum (A35670)
28 ALTSHLPFRK-----------------  D.Discoideum (U01064)
51 AVSGDEGWWTGQL---PSGRVGVFPSNYVA  H.sapiens (Z48615)
51 AVSGDEGWWTGQL---PSGRVGVFPSNYVA  Homo sapiens (Z48615)
26 ----------------------------SCIS  Human raf1(W13107)
26 ----------------------------SCIS  Human Raflkinase(R98215)
34 VQSEQKSRPS-----------------  Soybean kinase(M67449)
```

Fig. 3A

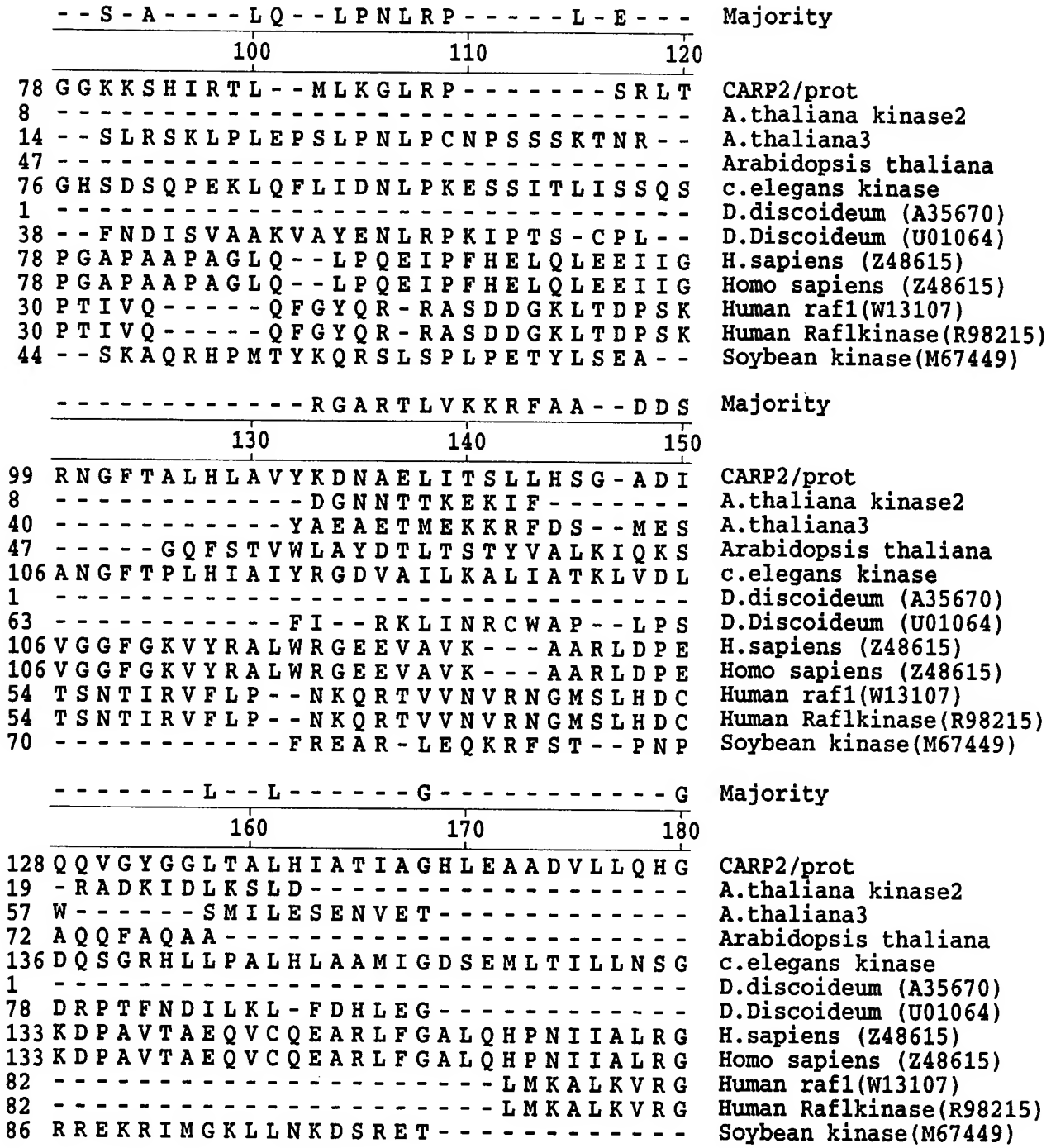
--S-A----LQ--LPNLRP-----L-E---
Majority
100
110
120
78 GGKKSHIRTL--MLKGLRP-------SRLT CARP2/prot
8 ---------- A.thaliana kinase2
14 --SLRSKLPLEPSLPNLPCNPSSSKTNR-- A.thaliana3
47 ---------- Arabidopsis thaliana
76 GHSDSQPEKLQFLIDNLPKESSITLISSQS c.elegans kinase
1 ---------- D.discoideum (A35670)
38 --FNDISVAAKVAYENLRPKIPTS-CPL-- D.Discoideum (U01064)
78 PGAPAAPAGLQ--LPQEIPFHELQLEEIIG H.sapiens (Z48615)
78 PGAPAAPAGLQ--LPQEIPFHELQLEEIIG Homo sapiens (Z48615)
30 PTIVQ-----QFGYQR-RASDDGKLTDPSK Human raf1(W13107)
30 PTIVQ-----QFGYQR-RASDDGKLTDPSK Human Raf1kinase(R98215)
44 --SKAQRHPMTYKQRSLSPLPETYLSEA-- Soybean kinase(M67449)
----------RGARTLVKKRFAA--DDS
Majority
130
140
150
99 RNGFTALHLAVYKDNAELITSLLHSG-ADI CARP2/prot
8 ----------DGNNTTKEKIF------- A.thaliana kinase2
40 ----------YAEAETMEKKRFDS--MES A.thaliana3
47 -----GQFSTVWLAYDTLTSTYVALKIQKS Arabidopsis thaliana
106 ANGFTPLHIAIYRGDVAILKALIATKLVDL c.elegans kinase
1 ---------- D.discoideum (A35670)
63 ----------FI--RKLINRCWAP--LPS D.Discoideum (U01064)
106 VGGFGKVYRALWRGEEVAVK---AARLDPE H.sapiens (Z48615)
106 VGGFGKVYRALWRGEEVAVK---AARLDPE Homo sapiens (Z48615)
54 TSNTIRVFLP--NKQRTVVNVRNGMSLHDC Human raf1(W13107)
54 TSNTIRVFLP--NKQRTVVNVRNGMSLHDC Human Raf1kinase(R98215)
70 ----------FREAR-LEQKRFST--PNP Soybean kinase(M67449)
-------L--L------G----------G
Majority
160
170
180
128 QQVGYGGLTALHIATIAGHLEAADVLLQHG CARP2/prot
19 -RADKIDLKSLD---------- A.thaliana kinase2
57 W------SMILESENVET---------- A.thaliana3
72 AQQFAQAA---------- Arabidopsis thaliana
136 DQSGRHLLPALHLAAMIGDSEMLTILLNSG c.elegans kinase
1 ---------- D.discoideum (A35670)
78 DRPTFNDILKL-FDHLEG---------- D.Discoideum (U01064)
133 KDPAVTAEQVCQEARLFGALQHPNIIALRG H.sapiens (Z48615)
133 KDPAVTAEQVCQEARLFGALQHPNIIALRG Homo sapiens (Z48615)
82 ----------LMKALKVRG Human raf1(W13107)
82 ----------LMKALKVRG Human Raf1kinase(R98215)
86 RREKRIMGKLLNKDSRET---------- Soybean kinase(M67449)

Fig. 3B

```
    ----------------------------R---  Majority
                  190       200       210
158 ANVNIQDAVFFTPLHIAAYYGHEQVTRLLL  CARP2/prot
30  ----------------------------  A.thaliana kinase2
69  ----------------------------  A.thaliana3
80  ------------LHEIEFLSAAADGDL--  Arabidopsis thaliana
166 ANIHVTDFVHFTALHCATYFGQENAVRTLI  c.elegans kinase
1   ----------------------------  D.discoideum (A35670)
95  ----------------------------  D.Discoideum (U01064)
163 ACLNPPHLCL-----VMEYARGGALSRVLA  H.sapiens (Z48615)
163 ACLNPPHLCLL----VMEYARGGALSRVLA  Homo sapiens (Z48615)
91  --LQPECCAVFRLLHE----HKGKKARLDW  Human raf1(W13107)
91  --LQPECCAVFRLLHE----HKGKKARLDW  Human Raf1kinase(R98215)
104 ----------------------------  Soybean kinase(M67449)

    ----------------------L-----  Majority
                  220       230       240
188 KFGADVNVSGEVGDRPLHLASAKGFLNIAK  CARP2/prot
30  ----------------------------  A.thaliana kinase2
69  ----------------------------  A.thaliana3
95  ------------DKTKCVVRLIDHFKHSG  Arabidopsis thaliana
196 SASANLNLGGAVNDRPIHLAAAKGLTSITK  c.elegans kinase
1   ----------------------------  D.discoideum (A35670)
95  ----------------------------K  D.Discoideum (U01064)
188 GRRVPPHV---LVNWAVQVARGMNYLHNDA  H.sapiens (Z48615)
188 GRRVPPHV---LVNWAVQVARGMNYLHNDA  Homo sapiens (Z48615)
115 NTDAASLIGEEL----------QVDFLDH--  Human raf1(W13107)
115 NTDAASLIGEEL----------QVDFLDH--  Human Raf1kinase(R98215)
104 ----------------------------K  Soybean kinase(M67449)

    ---L----------L---------KLA----  Majority
                  250       260       270
218 ---LLMEEGSKADVNAQDNEDHVPLHFCSR  CARP2/prot
30  ------------------RQLEKHLS----  A.thaliana kinase2
69  ----------------------------  A.thaliana3
112 P-----------------------NGQHLC--  Arabidopsis thaliana
226 ---LLLE--AKADPLLADDEGNQALHYAAK  c.elegans kinase
1   ----------------------------  D.discoideum (A35670)
96  ---LFFSSPGILRSLNNDQEVERELQ----  D.Discoideum (U01064)
215 PVPIIHRDLKSINILILEAIENHNLA----  H.sapiens (Z48615)
215 PVPIIHRDLKSINILILEAIENHNLA----  Homo sapiens (Z48615)
134 -VPLTTHNFARKTFL---------KLAFCD-  Human raf1(W13107)
134 -VPLTTHNFARKTFL---------KLAFCD-  Human Raf1kinase(R98215)
105 ------ESSSKSPSRSPNRQVKSKNR----  Soybean kinase(M67449)
```

Fig. 3C

```
        --------FL----------------Y---  Majority
                 280         290        300
245 FGHHDIVKYLLQSDLEVQPHVV--NIYG--  CARP2/prot
38  ----------------------------------  A.thaliana kinase2
69  ----------------------------------  A.thaliana3
119 ----MVLEFL----------------------  Arabidopsis thaliana
251 SGSLVILNMLIKQVRGTNDRICARNLYG--  c.elegans kinase
1   ----------------------------------  D.discoideum (A35670)
119 ----------------------------------  D.Discoideum (U01064)
241 DTVLKITDFGLAREWHKTTKMSAAGTYAWM  H.sapiens (Z48615)
241 DTVLKITDFGLAREWHKTTKMSAAGTYAWM  Homo sapiens (Z48615)
154 ----ICQKFLLNGFR------CQTCGYKFH  Human raf1(W13107)
154 ----ICQKFLLNGFR------CQTCGYKFH  Human Raf1kinase(R98215)
125 ----------------------------------  Soybean kinase(M67449)

        ------L-----K--VWS-ILQ-LL-----  Majority
                 310         320        330
271 -DTPLHLACYNGKFEVAKEIIQISGTESLT  CARP2/prot
38  ----------R--VWSRNLE------VN  A.thaliana kinase2
69  ----------WE----------AS  A.thaliana3
125 GDSLLRLIRYNQ----------------  Arabidopsis thaliana
279 -DTALHLSCYSGRLDIVKSILDSSPTNIVN  c.elegans kinase
1   ----------------------------------  D.discoideum (A35670)
119 ----------KKERFNEITEFLRGKK--  D.Discoideum (U01064)
271 APEVIRLSLFSKSSDVWS--FGVLLWELLT  H.sapiens (Z48615)
271 APEVIRLSLFSKSSDVWS--FGVLLWELLT  Homo sapiens (Z48615)
174 EHCSTKVP---TMCVDWSNIRQLLL-----  Human raf1(W13107)
174 EHCSTKVP---TMCVDWSNIRQLLL-----  Human Raf1kinase(R98215)
125 ----------KDSAWTKLLDNGGGKITA  Soybean kinase(M67449)

        -E----------------------------  Majority
                 340         350        360
300 KENIFSETAFHSACTYGKSIDLVKFLLDQN  CARP2/prot
48  PKA-------------------------  A.thaliana kinase2
73  KGE-------------------------  A.thaliana3
137 ----YKGLKLN------KVREICRCIL---  Arabidopsis thaliana
308 MENVFSETPLHAACTGGKSIELVSFLMKYP  c.elegans kinase
1   ----------------------------------  D.discoideum (A35670)
135 ----------------------------------  D.Discoideum (U01064)
299 GEVPYREID-ALAVAYG--VAMNKLTLPIP  H.sapiens (Z48615)
299 GEVPYREID-ALAVAYG--VAMNKLTLPIP  Homo sapiens (Z48615)
196 ----FPNSTI----GDSGVPALPSLTMR--  Human raf1(W13107)
196 ----FPNSTI----GDSGVPALPSLTMR--  Human Raf1kinase(R98215)
143 VET-------------------------  Soybean kinase(M67449)
```

Fig. 3D

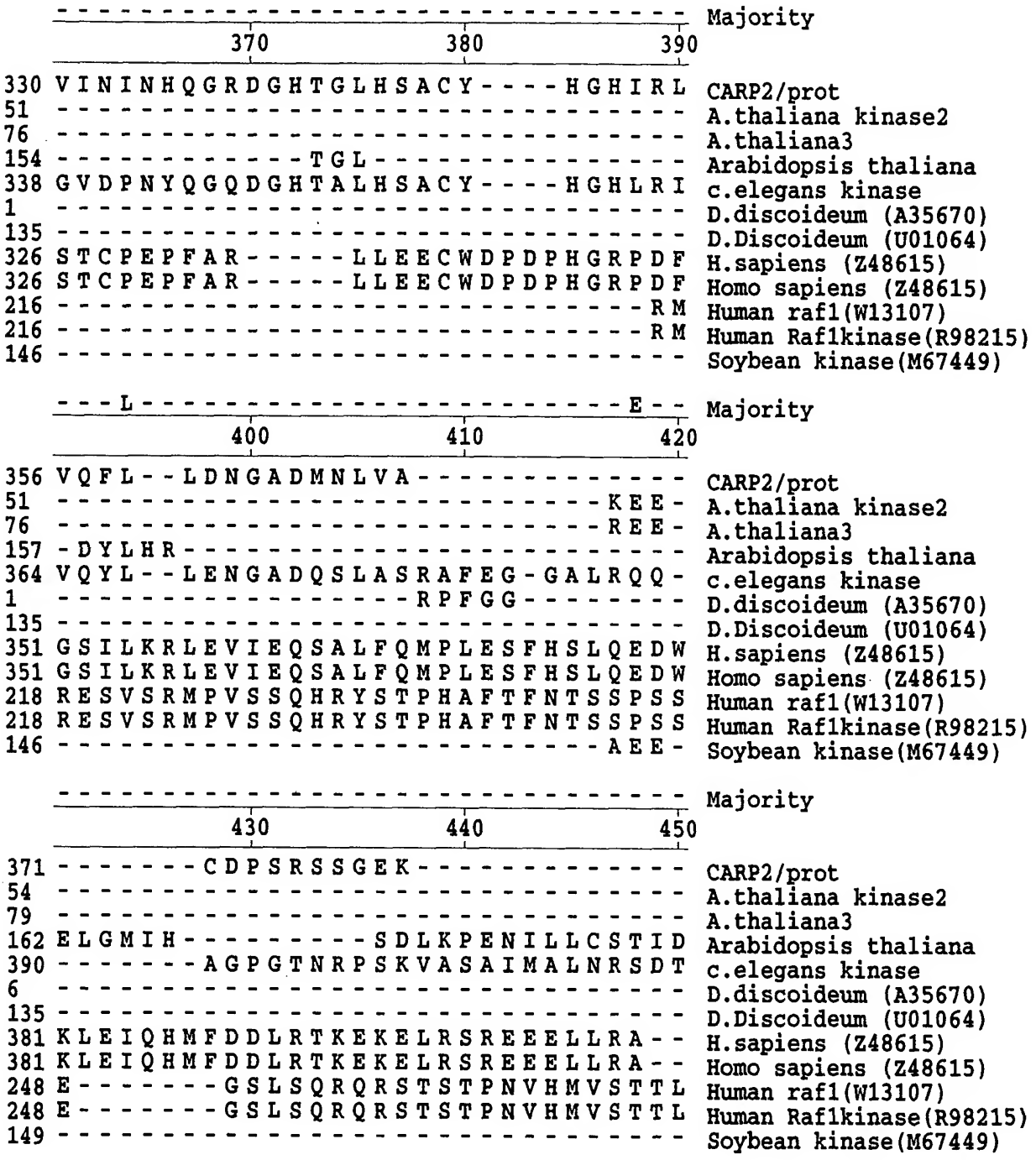
Majority
370 380 390
330 V I N I N H Q G R D G H T G L H S A C Y - - - - H G H I R L CARP2/prot
51 - A.thaliana kinase2
76 - A.thaliana3
154 - - - - - - - - - - - - - T G L - - - - - - - - - - - - - - - Arabidopsis thaliana
338 G V D P N Y Q G Q D G H T A L H S A C Y - - - - H G H L R I c.elegans kinase
1 - D.discoideum (A35670)
135 - D.Discoideum (U01064)
326 S T C P E P F A R - - - - - L L E E C W D P D P H G R P D F H.sapiens (Z48615)
326 S T C P E P F A R - - - - - L L E E C W D P D P H G R P D F Homo sapiens (Z48615)
216 - R M Human raf1(W13107)
216 - R M Human Raf1kinase(R98215)
146 - Soybean kinase(M67449)
Majority
400 410 420
356 V Q F L - - L D N G A D M N L V A - - - - - - - - - - - - CARP2/prot
51 - K E E - A.thaliana kinase2
76 - R E E - A.thaliana3
157 - D Y L H R - Arabidopsis thaliana
364 V Q Y L - - L E N G A D Q S L A S R A F E G - G A L R Q Q - c.elegans kinase
1 - - - - - - - - - - - - - - - - - - R P F G G - - - - - - - - D.discoideum (A35670)
135 - D.Discoideum (U01064)
351 G S I L K R L E V I E Q S A L F Q M P L E S F H S L Q E D W H.sapiens (Z48615)
351 G S I L K R L E V I E Q S A L F Q M P L E S F H S L Q E D W Homo sapiens (Z48615)
218 R E S V S R M P V S S Q H R Y S T P H A F T F N T S S P S S Human raf1(W13107)
218 R E S V S R M P V S S Q H R Y S T P H A F T F N T S S P S S Human Raf1kinase(R98215)
146 - A E E - Soybean kinase(M67449)
Majority
430 440 450
371 - - - - - - - - C D P S R S S G E K - - - - - - - - - - - - CARP2/prot
54 - A.thaliana kinase2
79 - A.thaliana3
162 E L G M I H - - - - - - - - - - S D L K P E N I L L C S T I D Arabidopsis thaliana
390 - - - - - - - - A G P G T N R P S K V A S A I M A L N R S D T c.elegans kinase
6 - D.discoideum (A35670)
135 - D.Discoideum (U01064)
381 K L E I Q H M F D D L R T K E K E L R S R E E E L L R A - - H.sapiens (Z48615)
381 K L E I Q H M F D D L R T K E K E L R S R E E E L L R A - - Homo sapiens (Z48615)
248 E - - - - - - - - G S L S Q R Q R S T S T P N V H M V S T T L Human raf1(W13107)
248 E - - - - - - - - G S L S Q R Q R S T S T P N V H M V S T T L Human Raf1kinase(R98215)
149 - Soybean kinase(M67449)

Fig. 3E

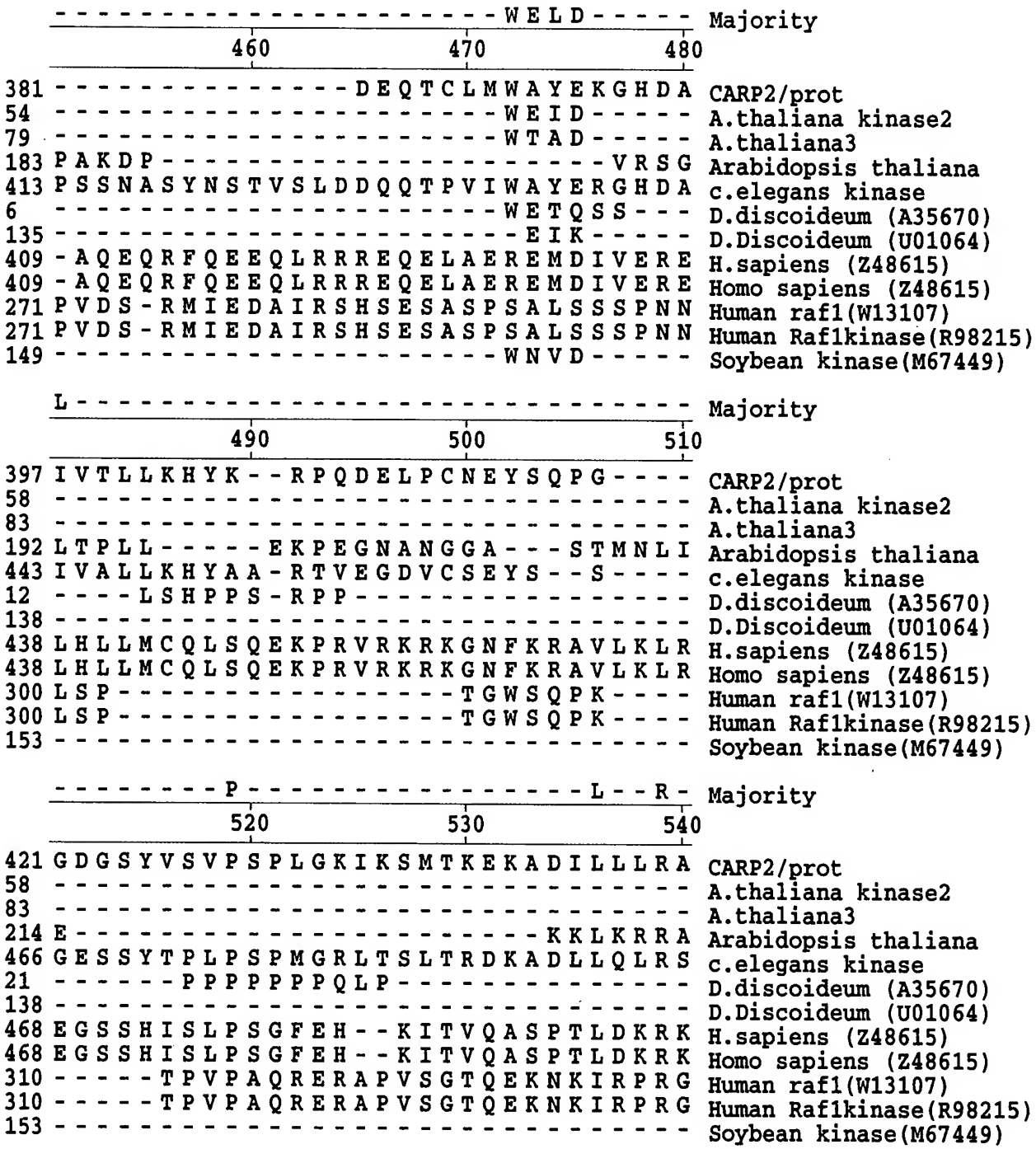
Majority
460
470
480
381 DEQTCLMWAYEKGHDA CARP2/prot
54 WEID A.thaliana kinase2
79 WTAD A.thaliana3
183 PAKDP VRSG Arabidopsis thaliana
413 PSSNASYNSTVSLDDQQTPVIWAYERGHDA c.elegans kinase
6 WETQSS D.discoideum (A35670)
135 EIK D.Discoideum (U01064)
409 AQEQRFQEEQLRRREQELAEREMDIVERE H.sapiens (Z48615)
409 AQEQRFQEEQLRRREQELAEREMDIVERE Homo sapiens (Z48615)
271 PVDS-RMIEDAIRSHSESASPSALSSSPNN Human raf1(W13107)
271 PVDS-RMIEDAIRSHSESASPSALSSSPNN Human Raf1kinase(R98215)
149 WNVD Soybean kinase(M67449)
Majority
490
500
510
397 IVTLLKHYK--RPQDELPCNEYSQPG CARP2/prot
58 A.thaliana kinase2
83 A.thaliana3
192 LTPLL-----EKPEGNANGGA---STMNLI Arabidopsis thaliana
443 IVALLKHYAA-RTVEGDVCSEYS--S c.elegans kinase
12 ----LSHPPS-RPP D.discoideum (A35670)
138 D.Discoideum (U01064)
438 LHLLMCQLSQEKPRVRKRKGNFKRAVLKLR H.sapiens (Z48615)
438 LHLLMCQLSQEKPRVRKRKGNFKRAVLKLR Homo sapiens (Z48615)
300 LSP TGWSQPK Human raf1(W13107)
300 LSP TGWSQPK Human Raf1kinase(R98215)
153 Soybean kinase(M67449)
Majority
520
530
540
421 GDGSYVSVPSPLGKIKSMTKEKADILLLRA CARP2/prot
58 A.thaliana kinase2
83 A.thaliana3
214 E KKLKRRA Arabidopsis thaliana
466 GESSYTPLPSPMGRLTSLTRDKADLLQLRS c.elegans kinase
21 PPPPPPQLP D.discoideum (A35670)
138 D.Discoideum (U01064)
468 EGSSHISLPSGFEH--KITVQASPTLDKRK H.sapiens (Z48615)
468 EGSSHISLPSGFEH--KITVQASPTLDKRK Homo sapiens (Z48615)
310 TPVPAQRERAPVSGTQEKNKIRPRG Human raf1(W13107)
310 TPVPAQRERAPVSGTQEKNKIRPRG Human Raf1kinase(R98215)
153 Soybean kinase(M67449)

Fig. 3F

```
    --D---------LSELEFGLRIGSGSFGTVY  Majority
                550       560       570
451 GLPSHF--HLQLSEIEFHEIIGSGSFGKVY  CARP2/prot
58  ----------LAKLETSNVIARGTYGTVY  A.thaliana kinase2
83  ----------LSQLFIGNKFASGAHSRIY  A.thaliana3
222 KRA-----------------------     Arabidopsis thaliana
496 ALPAPF--HLCLAEIEFQESIGSGSFGKVY  c.elegans kinase
81  -VRSEY--EIDFNELEFGQTIGKGFFGEVK  D.discoideum (A35670)
138 ----------FDEVAIVEKVGAGSFANVF  D.Discoideum (U01064)
496 GSDGAS--PPASPSIIPRLRAIRLTPVDCG  H.sapiens (Z48615)
496 GSDGAS--PPASPSIIPRLRAIRLTPVDCG  Homo sapiens (Z48615)
335 QRDSSYYWEIEASEVMLSTRIGSGSFGTVY  Human raf1(W13107)
335 QRDSSYYWEIEASEVMLSTRIGSGSFGTVY  Human Raf1kinase(R98215)
153 ----------MSQLFFGLKFAHGAHSRLY  Soybean kinase(M67449)

    KGIYRG-DVAVKILKRGDP--E-----K-E  Majority
                580       590       600
479 KGRCRNKIVAIKR-YRAN-----TYCSKSD  CARP2/prot
77  KGIYDGQDVAVKVLDWEDDGNETTAKTATN  A.thaliana kinase2
102 RGIYKQRAVAVKMVRIPTHKEETR--AKLE  A.thaliana3
225 ----------------------------  Arabidopsis thaliana
524 KGTYRGKLVAVKR-YRAM-----AFGCKSE  c.elegans kinase
58  RGYWRETDVAIKIIYRDQ------FKTKSS  D.discoideum (A35670)
157 LGIWNGYKVAIKILKNESISNDEK------  D.Discoideum (U01064)
524 GSSSGSSSGGSGTWSRGGPPKKEELVGGKK  H.sapiens (Z48615)
524 GSSSGSSSGGSGTWSRGGPPKKEELVGGKK  Homo sapiens (Z48615)
365 KGKWHG-DVAVKILKVVDPTPE--------Q  Human raf1(W13107)
365 KGKWHG-DVAVKILKVVDPTPE--------Q  Human Raf1kinase(R98215)
172 HGVYKDEAVAVKIIMVPEDDGNGALASRLE  Soybean kinase(M67449)

    KQ-FRNEVSVLSKLRHPNVVQFVGA-L---  Majority
                610       620       630
503 VDMFCREVSILCQLNHPCVIQFVGACL-N-  CARP2/prot
107 RALFRQEVTVWHKLNHPNVTKFVGASMGTT  A.thaliana kinase2
130 QQ-FKSEVALLSRLFHPNIVQFIAACK---  A.thaliana3
225 ----------VAKISERRVSMVTGE-----  Arabidopsis thaliana
548 TDMLCREVSILSRLAHPNVVAFVGTSL-D-  c.elegans kinase
82  LVMFQNEVGILSKLRHPNVVQFLGACTAG-  D.discoideum (A35670)
181 ---FIKEVSSLIKSHHPNVVTFMGA-----  D.Discoideum (U01064)
554 KGRTWGPSSTLQKERVGGEERLKG--LGEG  H.sapiens (Z48615)
554 KGRTWGPSSTLQKERVGGEERLKG--LGEG  Homo sapiens (Z48615)
387 FQAFRNEVAVLRKTRHVNILLFMGY-----  Human raf1(W13107)
387 FQAFRNEVAVLRKTRHVNILLFMGY-----  Human Raf1kinase(R98215)
202 KQ-FIREVTLLSRLHHQNVIKFSAACR---  Soybean kinase(M67449)
```

Fig. 3G

```
    ------------DPDHLCIVTEYLSGGSL Majority
                640       650       660
531 --------------DPSQFAIVTQYISGGSL CARP2/prot
137 NLNIRSADSKGSLPQQACCVVVEYLPGGTL A.thaliana kinase2
156 ----------------KPPVYCIITEYMSQGNL A.thaliana3
240 ---------------------------------- Arabidopsis thaliana
576 --------------DPSQFAIITEFVENGSL c.elegans kinase
111 --------------GEDHHCIVTEWMGGGSL D.discoideum (A35670)
203 ------------RIDPP--CIFTEYLQGGSL D.Discoideum (U01064)
582 SKQWSSSAPNLGKSPKHTPIAPGFASLNEM H.sapiens (Z48615)
582 SKQWSSSAPNLGKSPKHTPIAPGFASLNEM Homo sapiens (Z48615)
412 ------------MTKDNLAIVTQWCEGSSL Human raf1(W13107)
412 ------------MTKDNLAIVTQWCEGSSL Human Raf1kinase(R98215)
228 ----------------KPPVYCIITEYLAEGSL Soybean kinase(M67449)

    REHLH-ED-KFSLLP--------LKIALDI Majority
                670       680       690
548 FSLLHEQK---RILD--LQSK--LIIAVDV CARP2/prot
167 KQHLI-RHKSKKLAFKAV-----IKLALDL A.thaliana kinase2
173 RMYLN-KKEPYSLSIETV-----LRLALDI A.thaliana3
240 ---------------------------------- Arabidopsis thaliana
593 FRRENGERKNYRVMD--PAFR--LRISLDV c.elegans kinase
128 RQFLTDH---FNLLEQNPHIR--LKLALDI D.discoideum (A35670)
220 YDVLH--IQKIKLNPLMM-----YKMIHDL D.Discoideum (U01064)
612 EEFAEAEDGGSSVPPSPYSTPSYLSVPLPA H.sapiens (Z48615)
612 EEFAEAEDGGSSVPPSPYSTPSYLSVPLPA Homo sapiens (Z48615)
430 YKHLHVQETKFQMFQ--------LIDIARQT Human raf1(W13107)
430 YKHLHVQETKFQMFQ--------LIDIARQT Human Raf1kinase(R98215)
245 RAYLH-KLEHQTISLQKL-----IAFALDI Soybean kinase(M67449)

    ARGMEYLH---AQPIIHRDLKSHNILLDE- Majority
                700       710       720
571 AKGMEYLHN-LTQPIIHRDLNSHNILLY-- CARP2/prot
191 ARGLSYLH---SEKIVHRDVKTENMLLDAQ A.thaliana kinase2
197 SRGMEYLH---SQGVIHRDLKSNNLLLNDE A.thaliana3
240 ----------EASSKTEKSLDGIDM----- Arabidopsis thaliana
619 ARGMRYLHESAAKPVIHRDLNSHNILIH-- c.elegans kinase
153 AKGMNYLHGW-TPPILHRDLSSRNILLDHN D.discoideum (A35670)
243 SLGMEHLH---SIQMLHRDLTSKNILLDEF D.Discoideum (U01064)
642 EPSPGARAPWEPTPSAPPARWGHG----AR H.sapiens (Z48615)
642 EPSPGARAPWEPTPSAPPARWGHG----AR Homo sapiens (Z48615)
453 AQGMDYLH---AKNIIHRDMKSNNIFLHEG Human raf1(W13107)
453 AQGMDYLH---AKNIIHRDMKSNNIFLHEG Human Raf1kinase(R98215)
269 ARGMEYIH---SQGVIHRDLKPENILINED Soybean kinase(M67449)
```

Fig. 3H

```
    -RVK--------------IADFGLAR-LEA-  Majority
              730         740         750
598 ----------EDGHAVVADFGESRFLQS-  CARP2/prot
218 KNLK--------------IADFGVAR-VEA-  A.thaliana kinase2
224 MRVK--------------VADFGTSC-LET-  A.thaliana3
255 ----------------RCKVVDFGNAC----W  Arabidopsis thaliana
647 ----------ADGRSVVADFGESRFVCQ-  c.elegans kinase
182 IDPKNPLVSSRQDIKCKISDFGLSR-LKK-  D.discoideum (A35670)
270 KNIK--------------IADFGLA---TT-  D.Discoideum (U01064)
668 RRCDLALLGC-------ATLLGAVGLGAD-  H.sapiens (Z48615)
668 RRCDLALLGC-------ATLLGAVGLGAD-  Homo sapiens (Z48615)
480 LTVK--------------IGDFGLATVKSRW  Human raf1(W13107)
480 LTVK--------------IGDFGLATVKSRW  Human Raf1kinase(R98215)
296 NHLK--------------IADFGIAC-EEA-  Soybean kinase(M67449)

    LADDQAADGTGTLRWMAPEVFI--KGGPYS  Majority
              760         770         780
616 LDEDNMTKQPGNLRWMAPEVFT--QCTRYT  CARP2/prot
233 LNPKDMTGRTGTLGYMAPEV-I--DGKPYN  A.thaliana kinase2
239 -QCREAKGNMGTYRWMAPEM-I--KEKPYT  A.thaliana3
267 -ADKQFAEEIQTRQYRAPEVILK---SGYS  Arabidopsis thaliana
665 REDENLTKQPGNLRWMAPEVFS--QSGKYD  c.elegans kinase
210 EQASQMTQSVGCIPYMAPEVF---KGDSNS  D.discoideum (A35670)
283 LSDDMTLSGITNPRWRSPEL-T--KGLVYN  D.Discoideum (U01064)
690 VAEARAADGEEQRRWLDGLFFP--RAGRFP  H.sapiens (Z48615)
690 VAEARAADGEEQRRWLDGLFFP--RAGRFP  Homo sapiens (Z48615)
497 SGSQQVEQPTGSVLWMAPEVIRMQDNNPFS  Human raf1(W13107)
497 SGSQQVEQPTGSVLWMAPEVIRMQDNNPFS  Human Raf1kinase(R98215)
311 -SCDLLADDPGTYRWMAPEM-I--KRKSYG  Soybean kinase(M67449)

    RKVDVYSFGLVLWELVTGELPFAHLNP-VQ  Majority
              790         800         810
644 IKADVFSYALCLWEILTGEIPFAHLKP-AA  CARP2/prot
260 RRCDVYSFGICLWEIYCCDMPYPDLSF-VD  A.thaliana kinase2
265 RKVDVYSFGIVLWELTTALLPFQGMTP-VQ  A.thaliana3
293 FSVDMWSFGCTAFELVTGDMLFAPKDGN--  Arabidopsis thaliana
693 RKVDVFSFALVIWEIHTAELPFSHLKP-AA  c.elegans kinase
237 EKSDVYSYGMVLFELLTSDEPQQDMKP-MK  D.discoideum (A35670)
310 EKVDVYSFGLVVYEIYTGKIPFEGLDG-TA  D.Discoideum (U01064)
718 RGLSPPARPHGRREDVGPGLGLAPSATLVS  H.sapiens (Z48615)
718 RGLSPPARPHGRREDVGPGLGLAPSATLVS  Homo sapiens (Z48615)
527 FQSDVYSYGIVLYELMTGELPYSHINNRDQ  Human raf1(W13107)
527 FQSDVYSYGIVLYELMTGELPYSHINNRDQ  Human Raf1kinase(R98215)
337 KKVDVYSFGLILWEMLTGTIPYEDMNP-IQ  Soybean kinase(M67449)
```

Fig. 3I

```
    AAFAVAYGNARPPLPSDC----PAALSSLI Majority
                820         830         840
673 AAADMAYHHIRPPIGYS----IPKPISSLL CARP2/prot
289 VSSAVVLHNLRPEIPRCC----PTALAGIM A.thaliana kinase2
294 AAFAVAEKNERPPLPASC----QPALAHLI A.thaliana3
321 -----GYGEDEDHLA---------------- Arabidopsis thaliana
722 AAAEMTYKRGRPTLPNQPTAQFPAHILSLI c.elegans kinase
266 MAHLAAYESYRPPIPLTTSSKWKE----IL D.discoideum (A35670)
339 SAAKAAFENYRPAIPPDC----PVSLRKLI D.Discoideum (U01064)
748 LSSVSDCNSTRSLLRSDSDEAAPAAPSPPP H.sapiens (Z48615)
748 LSSVSDCNSTRSLLRSDSDEAAPAAPSPPP Homo sapiens (Z48615)
557 IIFMVGRGYASPDLSKLYKNC-PKAMKRLV Human raf1(W13107)
557 IIFMVGRGYASPDLSKLYKNC-PKAMKRLV Human Raf1kinase(R98215)
366 AAFAVVNKNSRPIIPSNC----PPAMRALI Soybean kinase(M67449)

    AQCWAPNPSKRPSFSEIV---LE-------- Majority
                850         860         870
699 IRGWNACPEGRPEFSEVVMK-LEECLCNIE CARP2/prot
315 KTCWDGNPQKRPEMKEVVKM-LEGV--DTS A.thaliana kinase2
320 KRCWSENPSKRPDFSNIVAV-LEKY--DEC A.thaliana3
331 ----------------LMMEL--------- Arabidopsis thaliana
752 PQAWHPESSSRPDFVEIV----------A c.elegans kinase
292 TQCWDSNPDSRPTFKQIIVH-LKE------ D.discoideum (A35670)
365 TKCWASDPSQRPSFTEILTE-LETM--KSK D.Discoideum (U01064)
778 SPP-APTPTPSPSTNPLVDLELESFKKDPR H.sapiens (Z48615)
778 SPP-APTPTPSPSTNPLVDLELESFKKDPR Homo sapiens (Z48615)
586 ADCVKKVKEERPLFPQIL----------- Human raf1(W13107)
586 ADCVKKVKEERPLFPQIL----------- Human Raf1kinase(R98215)
392 EQCWSLQPDKRPEFWQVVKI-LEQF--ES- Soybean kinase(M67449)

    ----P-SVTS--SLSL----TPS------- Majority
                880         890         900
728 L-MSPASSNSSGSLSP----SSSSDCLVNR CARP2/prot
342 K-GGGMIPE---------------------- A.thaliana kinase2
347 V-KEGLPLTSHASLTK----TKKA------ A.thaliana3
336 ----------------LGKMPRKIAIGGA---- Arabidopsis thaliana
771 L-LEPHVESTHTDISA----PSTV------ c.elegans kinase
315 --MEDQGVSSFASVPV----QT--------- D.discoideum (A35670)
392 F-IKQLSFLND--LIQ----NPD-------- D.Discoideum (U01064)
807 QSLTPTHVTAACAVSRGHRRTPSDGALGQR H.sapiens (Z48615)
807 QSLTPTHVTAACAVSRGHRRTPSDGALGQR Homo sapiens (Z48615)
604 ----------SSIELLQHSLPK----INR Human raf1(W13107)
604 ----------SSIELLQHSLPK----INR Human Raf1kinase(R98215)
418 ------SLASDGTLSL----VPNP------ Soybean kinase(M67449)
```

Fig. 3J

```
       -------H--------------------------  Majority
              910         920         930
753 GGPGRS-HVAALRSRFELEYALNARSYAAL  CARP2/prot
350 ---------------------------------  A.thaliana kinase2
366 ---------------------------------  A.thaliana3
349 ---KSKDYFDRHGDLKRIRRL----KYWPL  Arabidopsis thaliana
790 -----S-QLTSQWEQLSVA-PPPASKFPPI  c.elegans kinase
331 ---------------------------------  D.discoideum (A35670)
408 ---------------------------------  D.Discoideum (U01064)
837 GPPEPAGHGPGPRDLLDFPRLPDPQALFPA  H.sapiens (Z48615)
837 GPPEPAGHGPGPRDLLDFPRLPDPQALFPA  Homo sapiens (Z48615)
619 SASEPSLHRAAHTEDIN-------------  Human raf1(W13107)
619 SASEPSLHRAAHTEDIN-------------  Human Raf1kinase(R98215)
432 ---------------------------------  Soybean kinase(M67449)

       ------------LT-DP-KGP-------D  Majority
              940         950         960
782 SQSAGQYSS--QGLSLEEMKRSLQYTP-ID  CARP2/prot
350 ----------------DQSRGCFC-------  A.thaliana kinase2
366 ---------------ILDHLKGCVTSIS--S  A.thaliana3
372 DR----------LLIDKYKLPEAEAKEFA  Arabidopsis thaliana
813 LSALHGIAA--TG-TVEELRQR-------ID  c.elegans kinase
331 ---------------------------ID  D.discoideum (A35670)
408 ----------------DDYNNNLNYDEEVD  D.Discoideum (U01064)
867 RRRPPEFPGRPTTLTFAPRPRPAASRPRLD  H.sapiens (Z48615)
867 RRRPPEFPGRPTTLTFAPRPRPAASRPRLD  Homo sapiens (Z48615)
636 ----------ACTLTTSP------------  Human raf1(W13107)
636 ----------ACTLTTSP------------  Human Raf1kinase(R98215)
432 ----------------CWDHKKGLLHWIQKLG  Soybean kinase(M67449)

       PF---------L-I-P---P----------  Majority
              970         980         990
809 KY-------GYVSDPMSSMHFHSCRNSSSF  CARP2/prot
358 -F-------APARGP                  A.thaliana kinase2
380 PF-------SSSSVPVN-------------  A.thaliana3
391 EF----LTPILEFAPEKRPTAQQC-----L  Arabidopsis thaliana
834 NN-------GYVIN----------------  c.elegans kinase
333 TG-------VY--------------------  D.discoideum (A35670)
422 S                               D.Discoideum (U01064)
897 PWKLVSFGRTLTISPPSRPDTPESPGPPSV  H.sapiens (Z48615)
897 PWKLVSFGRTLTISPPSRPDTPESPGPPSV  Homo sapiens (Z48615)
644 --RLPVF                         Human raf1(W13107)
644 --RLPVF                         Human Raf1kinase(R98215)
448 PL-------HQNSGPVPKPKF---------  Soybean kinase(M67449)
```

Fig. 3K

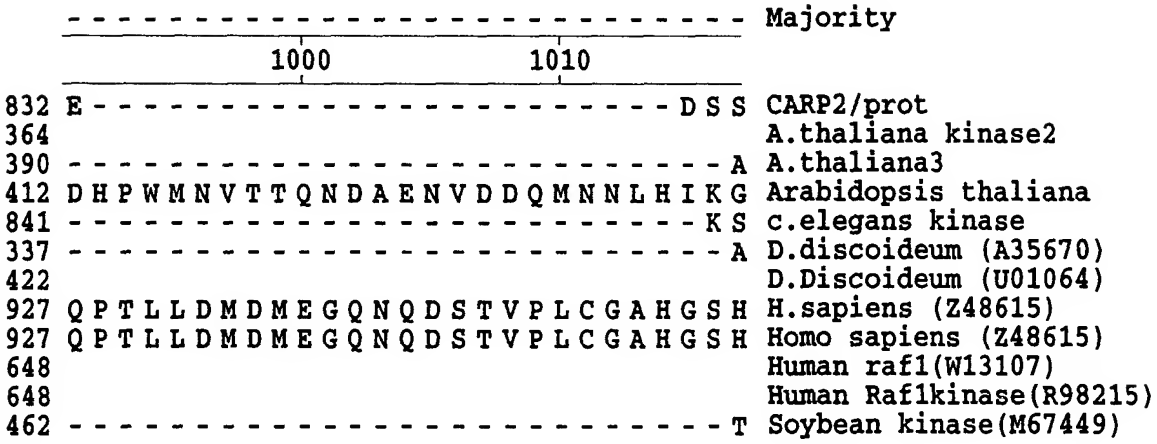
Majority
1000
1010
832 E - D S S CARP2/prot
364 A.thaliana kinase2
390 - A A.thaliana3
412 D H P W M N V T T Q N D A E N V D D Q M N N L H I K G Arabidopsis thaliana
841 - K S c.elegans kinase
337 - A D.discoideum (A35670)
422 D.Discoideum (U01064)
927 Q P T L L D M D M E G Q N Q D S T V P L C G A H G S H H.sapiens (Z48615)
927 Q P T L L D M D M E G Q N Q D S T V P L C G A H G S H Homo sapiens (Z48615)
648 Human raf1(W13107)
648 Human Raf1kinase(R98215)
462 - T Soybean kinase(M67449)

Fig. 3L

```
Protein Family / Domain Matches, HMMer version 2
Searching for complete domains
hmmpfam - search a single seq against HMM database
HMMER 2.1.1 (Dec 1998)
Copyright (C) 1992-1998 Washington University School of Medicine
HMMER is freely distributed under the GNU General Public License (GPL).
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
HMM file:                 /prod/ddm/seqanal/PFAM/pfam3.4/Pfam
Sequence file:            /tmp/orfanal.13255.aa
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
 Query:  sequence13252
Scores for sequence family classification (score includes all domains):
Model    Description                                        Score    E-value  N
-------- -----------
ank      PF00023 Ank repeat                                 207.5      2e-58  9
pkinase  PF00069 Eukaryotic protein kinase domain           201.9    9.9e-57  1

Parsed for domains:
Model    Domain  seq-f seq-t    hmm-f hmm-t       score  E-value
-------- ------- ----- -----    ----- -----       -----  -------
ank        1/9      66    99 ..     1    33 []     3.2       12
ank        2/9     100   132 ..     1    33 []    34.0  3.4e-06
ank        3/9     133   165 ..     1    33 []    44.5  2.4e-09
ank        4/9     168   198 ..     1    33 []    34.6  2.3e-06
ank        5/9     199   233 ..     1    33 []    28.1  0.00021
ank        6/9     234   268 ..     1    33 []    15.4     0.28
ank        7/9     269   302 ..     1    33 []    20.6    0.037
ank        8/9     306   338 ..     1    33 []     3.3       11
ank        9/9     339   371 ..     1    33 []    35.4  1.3e-06
pkinase    1/1     463   716 ..     1   273 [.   201.9  9.9e-57
Alignments of top-scoring domains:
ank: domain 1 of 9, from 66 to 99: score 3.2, E = 12
                    *->nGnTPLHlAaryg.nvevvklLLehGAdvnartk<-*
                       nG++ LHl+++ g++ + ++ L+ +G  +   t+
  sequence13     66    NGLSLLHLCCICGgKKSHIRTLMLKGLRPSRLTR    99

ank: domain 2 of 9, from 100 to 132: score 34.0, E = 3.4e-06
                    *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                       nG+T+LHlA++++n e++  LL  GAd+  + +
  sequence13    100    NGFTALHLAVYKDNAELITSLLHSGADIQQVGY    132

ank: domain 3 of 9, from 133 to 165: score 44.5, E = 2.4e-09
                    *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                        G+T+LH+A ++g++e +++LL+hGA+vn+++
  sequence13    133    GGLTALHIATIAGHLEAADVLLQHGANVNIQDA    165

ank: domain 4 of 9, from 168 to 198: score 34.6, E = 2.3e-06
                    *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                         +TPLH+Aa+yg+ +v +lLL+ GAdvn+  +
  sequence13    168    --FTPLHIAAYYGHEQVTRLLLKFGADVNVSGE    198

ank: domain 5 of 9, from 199 to 233: score 28.1, E = 0.00021
                    *->nGnTPLHlAarygnvevvklLLe..hGAdvnartk<-*
                        G+ PLHlA+ +g ++++klL+e++  Advna+++
  sequence13    199    VGDRPLHLASAKGFLNIAKLLMEegSKADVNAQDN    233
```

Fig. 4A

```
ank: domain 6 of 9, from 234 to 268: score 15.4, E = 0.28
                  *->nGnTPLHlAarygnvevvklLLe..hGAdvnartk<-*
                       + PLH ++r g+ ++vk+LL+++    ++++++
  sequence13   234    EDHVPLHFCSRFGHHDIVKYLLQsdLEVQPHVVNI    268

ank: domain 7 of 9, from 269 to 302: score 20.6, E = 0.037
                  *->nGnTPLHlAarygnvevvklLLe.hGAdvnartk<-*
                      G+TPLHlA+++g+ ev+k  ++  G+    + +
  sequence13   269    YGDTPLHLACYNGKFEVAKEIIQiSGTESLTKEN    302

ank: domain 8 of 9, from 306 to 338: score 3.3, E = 11
                  *->nGnTPLHlAaryg.nvevvklLLe.hGAdvnartk<-**
                        T+ H A+ yg+++++vk+LL+++  ++n + +
  sequence13   306    --ETAFHSACTYGkSIDLVKFLLDqNVININHQGR    338

ank: domain 9 of 9, from 339 to 371: score 35.4, E = 1.3e-06
                  *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                     +G+T LH A+++g++++v++LL++GAd n +
  sequence13   339    DGHTGLHSACYHGHIRLVQFLLDNGADMNLVAC    371

pkinase: domain 1 of 1, from 463 to 716: score 201.9, E = 9.9e-57
                  *->yelleklGeGsfGkVykakhktgkivAvKilk......kesls..lr
                     +e++e++G+GsfGkVyk++ + +kivA+K  + ++  +k++++   r
  sequence13   463    IEFHEIIGSGSFGKVYKGRCR-NKIVAIKRYRantycsKSDVDmfCR 508

                     Eiqilkrlsl-pNIvrllgvfedtddhlylvmEymegGdLfdylrrng.pl
                     E++il +l+Hp ++++ g++ ++++ + +v++y  gG+Lf++l+++++ l
  sequence13   509 EVSILCQLNHPCVIQFVGAVLNDPSQFAIVTQYISGGSLFSLLHEQKrIL 558

                     sekeakkialQilrGleYLHsng..ivHRDLKpeNILldengtvKiaDFG
                     + +  + ia ++++G+eYLH+  ++i+HRDL + NILl e+g+  +aDFG
  sequence13   559 DLQSKLIIAVDVAKGMEYLHNLTqpIIHRDLNSHNILLYEDGHAVVADFG 608

                     LArll.....eklttfvGTpwYmmAPEvileg.rgysskvDvWSlGviLy
                      +r+l++ ++ ++t   G +++m APEv   + + y+ k+Dv S+   L+
  sequence13   609 ESRFLqsldeDNMTKQPGNLRWM-APEV-FTQcTRYTIKADVFSYALCLW 656

                     ElltggplfpgadlpaftggdevdqliifvlklPfsdelpktridpleel
                     E+ltg                          ++Pf +       +p ++
  sequence13   657 EILTG-------------------------EIPFAH------LKPAAAA 674

                     frikkr..rlplpsncSeelkdLlkkcLnkDPskRpGsatakeil<-*
                      ++ +++ r+p+ ++++++  +Ll + +n  P+ Rp    + e++
  sequence13   675 ADMAYHhiRPPIGYSIPKPISSLLIRGWNACPEGRP---EFSEVV    716
```

Fig. 4B

```
gtcgacccac gcgtccggtg aagggcagca gcacaggaga aaagcaaaga cttctttaaa   60

atg ggg aat tac aaa tcc aga cca aca cag act tgt tct gat gaa tgg   108
Met Gly Asn Tyr Lys Ser Arg Pro Thr Gln Thr Cys Ser Asp Glu Trp
  1               5                  10                  15

aag aag aaa gtt agt gaa tct tac gct att atc ata gaa agg ctg gag   156
Lys Lys Lys Val Ser Glu Ser Tyr Ala Ile Ile Ile Glu Arg Leu Glu
            20                  25                  30

gat aac ctg cag atc aaa gaa aat gaa ttt caa gaa cta agg cac atc   204
Asp Asn Leu Gln Ile Lys Glu Asn Glu Phe Gln Glu Leu Arg His Ile
        35                  40                  45

ttt ggc tct gat gaa gcc ttc agt gaa gtc agt tta aat tac cgc aca   252
Phe Gly Ser Asp Glu Ala Phe Ser Glu Val Ser Leu Asn Tyr Arg Thr
    50                  55                  60

gag cgt ggc ctg tcc ctg cta cac ctc tgc tgt gtc tgt ggc ggc aac   300
Glu Arg Gly Leu Ser Leu Leu His Leu Cys Cys Val Cys Gly Gly Asn
65                  70                  75                  80

aag tca cat atc cgt gcc ctt atg tta aaa ggg ctc cgt cca tcc aga   348
Lys Ser His Ile Arg Ala Leu Met Leu Lys Gly Leu Arg Pro Ser Arg
                85                  90                  95

ctg acg aga aat ggg ttt cca gct ctg cac ctg gcc gtt tac aag gac   396
Leu Thr Arg Asn Gly Phe Pro Ala Leu His Leu Ala Val Tyr Lys Asp
            100                 105                 110

agc ccg gaa ctt atc act tca ctg ttg cac agc gga gca gat gtt cag   444
Ser Pro Glu Leu Ile Thr Ser Leu Leu His Ser Gly Ala Asp Val Gln
        115                 120                 125

caa gtg gga tac ggt ggc ctc aca gcc ctc cac ata gct gca ata gct   492
Gln Val Gly Tyr Gly Gly Leu Thr Ala Leu His Ile Ala Ala Ile Ala
    130                 135                 140

gga cac cca gag gct gca gaa gtg ctg cta caa cat ggg gcc aat gtg   540
Gly His Pro Glu Ala Ala Glu Val Leu Leu Gln His Gly Ala Asn Val
145                 150                 155                 160

aat gtt caa gat gcc gtc ttc ttc acc cca ctg cac att gca gcc tac   588
Asn Val Gln Asp Ala Val Phe Phe Thr Pro Leu His Ile Ala Ala Tyr
                165                 170                 175

tat ggg cac gag cag gta acc agt gtc ctt ttg aag ttt ggt gct gat   636
Tyr Gly His Glu Gln Val Thr Ser Val Leu Leu Lys Phe Gly Ala Aspp
            180                 185                 190

gtc aat gta agc ggt gaa gtt ggg gac agg cct ctg cac ctg gcc tct   684
Val Asn Val Ser Gly Glu Val Gly Asp Arg Pro Leu His Leu Ala Ser
        195                 200                 205
```

Fig. 5A

```
gca aag ggc ttc ttc aac att gtg aaa ctc ctg gta gaa gaa ggg agc   732
Ala Lys Gly Phe Phe Asn Ile Val Lys Leu Leu Val Glu Glu Gly Ser
    210                 215                 220

aaa gca gat gtg aac gct cag gac aat gaa gac cac gtc cct ctg cac   780
Lys Ala Asp Val Asn Ala Gln Asp Asn Glu Asp His Val Pro Leu His
225                 230                 235                 240

ttc tgt tct cga ttt gga cac cac aat ata gtg agc tac ctg ctc cag   828
Phe Cys Ser Arg Phe Gly His His Asn Ile Val Ser Tyr Leu Leu Gln
                245                 250                 255

agt gac tta gag gtc cag cct cac gtc att aac atc tat ggt gac act   876
Ser Asp Leu Glu Val Gln Pro His Val Ile Asn Ile Tyr Gly Asp Thr
            260                 265                 270

cct ttg cac ctg gca tgc tac aat gga aat ttt gaa gtt gcc aag gaa   924
Pro Leu His Leu Ala Cys Tyr Asn Gly Asn Phe Glu Val Ala Lys Glu
        275                 280                 285

att gtc cag gta aca gga act gaa agt ctg act aag gaa aac atc ttc   972
Ile Val Gln Val Thr Gly Thr Glu Ser Leu Thr Lys Glu Asn Ile Phe
    290                 295                 300

agc gag aca gct ttt cac agt gct tgt acc tat ggc aag aac att gac   1020
Ser Glu Thr Ala Phe His Ser Ala Cys Thr Tyr Gly Lys Asn Ile Asp
305                 310                 315                 320

ctg gtc aaa ttt ctt ctt gat cag aat gct gtg aac att aac cac cga   1068
Leu Val Lys Phe Leu Leu Asp Gln Asn Ala Val Asn Ile Asn His Arg
                325                 330                 335

gga aga gat ggg cac aca gga ttg cac tct gct tgc tac cac ggc cat   1116
Gly Arg Asp Gly His Thr Gly Leu His Ser Ala Cys Tyr His Gly His
            340                 345                 350

atc cgc ctg gtt cag ttc cta ctt gat aat ggt gca gat atg aat ctt   1164
Ile Arg Leu Val Gln Phe Leu Leu Asp Asn Gly Ala Asp Met Asn Leu
        355                 360                 365

gtc gct tgt gat ccc agc agg tct agt ggt gaa aaa gat gag cag aca   1212
Val Ala Cys Asp Pro Ser Arg Ser Ser Gly Glu Lys Asp Glu Gln Thr
    370                 375                 380

tgt ttg atg tgg gct tac gag aaa gga cat gat gcc att gtt aca ctc   1260
Cys Leu Met Trp Ala Tyr Glu Lys Gly His Asp Ala Ile Val Thr Leu
385                 390                 395                 400

ctg aag cac tac aag aga ccc cag gag gag ctg cca tgt aac gaa tat   1308
Leu Lys His Tyr Lys Arg Pro Gln Glu Glu Leu Pro Cys Asn Glu Tyr
                405                 410                 415

tcc cag cct gga gga gat ggc tcc tat gtg tct gtt cct tcc ccc ttg   1356
Ser Gln Pro Gly Gly Asp Gly Ser Tyr Val Ser Val Pro Ser Pro Leu
            420                 425                 430
```

Fig. 5B

```
ggc aag att aaa agc atg aca aaa gag aag gca gat gtt ctc ctc ctg   1404
Gly Lys Ile Lys Ser Met Thr Lys Glu Lys Ala Asp Val Leu Leu Leu
        435                 440                 445

agg gct gaa cta ccc tcc cgc ttc cat ctc caa ctc tcc gaa atc gag   1452
Arg Ala Glu Leu Pro Ser Arg Phe His Leu Gln Leu Ser Glu Ile Glu
    450                 455                 460

ttc cac gag att atc ggc tcg ggt tcc ttt ggg aaa gtc tat aaa ggg   1500
Phe His Glu Ile Ile Gly Ser Gly Ser Phe Gly Lys Val Tyr Lys Gly
465                 470                 475                 480

cga tgc aga aat aaa ata gtg gcg atc aaa cga tac cga gcc aac acc   1548
Arg Cys Arg Asn Lys Ile Val Ala Ile Lys Arg Tyr Arg Ala Asn The
                485                 490                 495

tac tgc tcc aag tca gac gtg gat atg ttt tgc cga gag gtg tcc att   1596
Tyr Cys Ser Lys Ser Asp Val Asp Met Phe Cys Arg Glu Val Ser Ile
            500                 505                 510

ctc tgc cag ctc aac cac ccc tgc gtg gtt cag ttt gtg ggt gcc tgc   1644
Leu Cys Gln Leu Asn His Pro Cys Val Val Gln Phe Val Gly Ala Cys
        515                 520                 525

ctg gat gac ccc agt cag ttt gcc att gtc act cag tac att tca gga   1692
Leu Asp Asp Pro Ser Gln Phe Ala Ile Val Thr Gln Tyr Ile Ser Gly
    530                 535                 540

ggc tcc ctg ttc tcc ctg ctt cat gaa cag aag aga att ctt gac ttg   1740
Gly Ser Leu Phe Ser Leu Leu His Glu Gln Lys Arg Ile Leu Asp Leu
545                 550                 555                 560

cag tct aaa tta atc att gcg gta gac gtt gcc aag ggc atg gag tac   1788
Gln Ser Lys Leu Ile Ile Ala Val Asp Val Ala Lys Gly Mey Glu Tyr
                565                 570                 575

ctg cac agc ttg acc cag cca atc ata cac cgc gac ctg aac agc cac   1836
Leu His Ser Leu Thr Gln Pro Ile Ile His Arg Asp Leu Asn Ser His
            580                 585                 590

aat att ctg ctc tat gag gat ggc cat gct gtg gtg gca gat ttt gga   1884
Asn Ile Leu Leu Tyr Glu Asp Gly His Ala Val Val Ala Asp Phe Gly
        595                 600                 605

gaa tca aga ttt ctg cag tcc ctg gat gaa gac aac atg aca aag cag   1932
Glu Ser Arg Phe Leu Gln Ser Leu Asp Glu Asp Asn Met Thr Lys Gln
    610                 615                 620

cca ggg aac ctg cgc tgg atg gcc cct gag gtg ttc aca cag tgc acg   1980
Pro Gly Asn Leu Arg Trp Met Ala Pro Glu Val Phe Thr Gln Cys Thr
625                 630                 635                 640

aga tac acc atc aag gct gat gtc ttc agt tac tcc ctg tgt ctg tgg   2028
Arg Tyr Thr Ile Lys Ala Asp Val Phe Ser Tyr Ser Leu Cys Leu Trp
                645                 650                 655
```

Fig. 5C

```
gag ctc ctc act gga gaa att cca ttc gct cat ctc aag cca gcc gct   2076
Glu Leu Leu Thr Gly Glu Ile Pro Phe Ala His Leu Lys Pro Ala Ala
            660                 665                 670

gca gca gca gat atg gcg tat cac cac atc aga ccg ccc atc ggc tat   2124
Ala Ala Ala Asp Met Ala Tyr His His Ile Arg Pro Pro Ile Gly Tyr
        675                 680                 685

tcc atc ccc aag ccc atc tca tcc ctg ctg ata cgg ggc tgg aat gca   2172
Ser Ile Pro Lys Pro Ile Ser Ser Leu Leu Ile Arg Gly Trp Asn Ala
    690                 695                 700

tgt cct gaa gga cga cca gag ttc tct gaa gtc gtt agc aaa ctg gag   2220
Cys Pro Glu Gly Arg Pro Glu Phe Ser Glu Val Val Ser Lys Leu Glu
705                 710                 715                 720

gag tgc cta tgc aat gtg gag ctc atg tct cca gca tca agt aac agc   2268
Glu Cys Leu Cys Asn Val Glu Leu Met Ser Pro Ala Ser Ser Asn Ser
                725                 730                 735

agt ggc tct ctg tca cct tcc tct tct tcc gat tgc ctg ctg agc cgg   2316
Ser Gly Ser Leu Ser Pro Ser Ser Ser Ser Asp Cys Leu Leu Ser Arg
            740                 745                 750

gga ggg cct ggc cgg agc cac gtg gca gcc tta cgg agc cgt ttt gag   2364
Gly Gly Pro Gly Arg Ser His Val Ala Ala Leu Arg Ser Arg Phe Glu
        755                 760                 765

ttg gag tat gcc cta aat gca agg tcc tat gct ggg tgg tcc caa agt   2412
Leu Glu Tyr Ala Leu Asn Ala Arg Ser Tyr Ala Gly Trp Ser Gln Ser
    770                 775                 780

gtt gga aca cac tct aat ccg ggc ctg tct ttg gag gag atg aat agg   2460
Val Gly Thr His Ser Asn Pro Gly Leu Ser Leu Glu Glu Met Asn Arg
785                 790                 795                 800

agc acc cag tat tca act gtt gac aaa tac ggc tat gtg tct gat ccc   2508
Ser Thr Gln Tyr Ser Thr Val Asp Lys Tyr Gly Tyr Val Ser Asp Pro
                805                 810                 815

atg agc ctg acg cac ctt cac tcc cgc caa gac gac agc aac ttt gag   2556
Met Ser Leu Thr His Leu His Ser Arg Gln Asp Asp Ser Asn Phe Glu
            820                 825                 830

gac agc aac tgacaggtct ggcatacacc taaggggcgt ctccccatca           2605
Asp Ser Asn
        835

ggctgacagc agtgatttta cccatggcag gcttgcttcc aattataacg ccctgccctc 2665
tgaggtttct tcaaatcgtc ttgcttattc taagctcgtt taattccctt ctacaggaca 2725
ggctttgact catgccaagc ctgaagtgtc aaagagcaga tacagaatgt gcatgaggaa 2785
ttgttcttag tttgatattt aaagccctta attgcctggg gctggggttc aaatctgtgt 2845
agatagctgg gttgaccctt atgtatttgt agaccaaact gtgtgggctt gtgtttgagg 2905
gtctcctgtt gggtttctta aaaacaagct ggctgattta tctcctgttg cctttgttgt 2965
tacttctgtg attaaagtct cttcggtgat ctagaaaaaa aaaaaaaaaa agggcggccg 3025
c                                                                  3026
```

Fig. 5D

```
Searching for complete domains in PFAM
hmmpfam - search a single seq against HMM database
HMMER 2.1.1 (Dec 1998)
Copyright (C) 1992-1998 Washington University School of Medicine
HMMER is freely distributed under the GNU General Public License (GPL).
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
HMM file:                 /prod/ddm/seqanal/PFAM/pfam4.4/Pfam
Sequence file:            /prod/ddm/wspace/orfanal/oa-script.11086.seq
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
 Query:  ratCARKpro

Scores for sequence family classification (score includes all domains):
Model    Description                                        Score    E-value  N
-------- -----------                                        -----    ------- ---
ank        Ank repeat                                       212.7    5.5e-60  9
pkinase    Eukaryotic protein kinase domain                 206.4    4.3e-58  1

Parsed for domains:
Model    Domain  seq-f seq-t    hmm-f hmm-t       score  E-value
-------- ------- ----- -----    ----- -----       -----  -------
ank        1/9      66    99 ..     1    33 []     1.2       48
ank        2/9     100   132 ..     1    33 []    28.6  0.00014
ank        3/9     133   165 ..     1    33 []    49.2  9.1e-11
ank        4/9     168   198 ..     1    33 []    31.9  1.4e-05
ank        5/9     199   233 ..     1    33 []    28.4  0.00017
ank        6/9     234   264 ..     1    33 []    12.6     2.4
ank        7/9     269   302 ..     1    33 []    23.1   0.0064
ank        8/9     306   338 ..     1    33 []    11.2     3.5
ank        9/9     339   371 ..     1    33 []    36.4  6.5e-07
pkinase    1/1     463   716 ..     1   273.[.   206.4  4.3e-58

Alignments of top-scoring domains:
ank: domain 1 of 9, from 66 to 99: score 1.2, E = 48
                    *->nGnTPLHlAaryg.nvevvklLLehGAdvnartk<-*
                       +G++ LHl++  g+n + +++L+ +G  +   t+
  ratCARKpro     66    RGLSLLHLCCVCGgNKSHIRALMLKGLRPSRLTR    99

ank: domain 2 of 9, from 100 to 132: score 28.6, E = 0.00014
                    *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                       nG+ +LHlA+++++ e++  LL  GAdv  + +
  ratCARKpro    100    NGFPALHLAVYKDSPELITSLLHSGADVQQVGY    132

ank: domain 3 of 9, from 133 to 165: score 49.2, E = 9.1e-11
                    *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                         G+T+LH+Aa++g+ e +++LL+hGA+vn+++
  ratCARKpro    133    GGLTALHIAAIAGHPEAAEVLLQHGANVNVQDA    165

ank: domain 4 of 9, from 168 to 198: score 31.9, E = 1.4e-05
                    *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                          +TPLH+Aa+yg+ +v  +LL+ GAdvn+  +
  ratCARKpro    168    --FTPLHIAAYYGHEQVTSVLLKFGADVNVSGE    198

ank: domain 5 of 9, from 199 to 233: score 28.4, E = 0.00017
                    *->nGnTPLHlAarygnvevvklLLe..hGAdvnartk<-*
                       G+ PLHlA+ +g  ++vklL+e++  Advna+++
  ratCARKpro    199    VGDRPLHLASAKGFFNIVKLLVEegSKADVNAQDN    233
```

Fig. 6A

```
ank: domain 6 of 9, from 234 to 264: score 12.6, E = 2.4
                  *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                       + PLH ++r g+ ++v +LL+  +d  ++
  ratCARKpro   234    EDHVPLHFCSRFGHHNIVSYLLQ--SDLEVQPH    264

ank: domain 7 of 9, from 269 to 302: score 23.1, E = 0.0064
                  *->nGnTPLHlAarygnvevvklLLe.hGAdvnartk<-*
                      G+TPLHlA+++gn ev+k  ++  G+    + +
  ratCARKpro   269    YGDTPLHLACYNGNFEVAKEIVQvTGTESLTKEN    302

ank: domain 8 of 9, from 306 to 338: score 11.2, E = 3.5
                  *->nGnTPLHlAatyg.nvevvklLLe.hGAdvnartk<-*
                        T+ H A+ yg+n+++vk+LL+++  ++n r +
  ratCARKpro   306    --ETAFHSACTYGkNIDLVKFLLDqNAVNINHRGR    338

ank: domain 9 of 9, from 339 to 371: score 36.4, E = 6.5e-07
                  *->nGnTPLHlAarygnvevvklLLehGAdvnartk<-*
                     +G+T LH A+++g++++v++LL++GAd n +
  ratCARKpro   339    DGHTGLHSACYHGHIRLVQFLLDNGADMNLVAC    371

pkinase: domain 1 of 1, from 463 to 716: score 206.4, E = 4.3e-58
                  *->yelleklGeGsfGkVykakhktgkivAvKilk......kesls..lr
                     +e++e++G+GsfGkVyk++ + +kivA+K  + ++  +k++++   r
  ratCARKpro   463    IEFHEIIGSGSFGKVYKGRCR-NKIVAIKRYRantycsKSDVDmfCR 508

                     EiqilkrlsdpnivrllgvfedtddhlylvmEymegGdLfdylrrng.pl
                     E++il +l+Hp +v++ g++ d+++ + +v++y  gG+lf++l+++++ l
  ratCARKpro   509 EVSILCQLNHPCVVQFVGACLDDPSQFAIVTQYISGGSLFSLLHEQHrIL 558

                     sekeakkialQilrGleYLHsng..ivHRDLKpeNILldengtvKiaDFG
                     + +  + ia ++++G+eYLHs  ++i+HRDL + NILl e+g+  +aDFG
  ratCARKpro   559 DLQSKLIIAVDVAKGMEYLHSLTqpIIHRDLNSHNILLYEDGHAVVADFG 608

                     LArll.....eklttfvGTpwYmmAPEvileg.rgysskvDvWSlGviLy
                      +r+l++ ++ ++t   G +++m APEv   + + y+ k+Dv S+   L+
  ratCARKpro   609 ESRFLqsldeDNMTKQPGNLRWM-APEV-FTQcTRYTIKADVFSYSLCLW 656

                     ElltggplfpgadlpaftggdevdqliifvlklPfsdelpktridpleel


                     Elltg                          ++Pf +       +p ++
  ratCARKpro   657 ELLTG-------------------------EIPFAH------LKPAAAA 674

                     frikkr..rlplpsncSeelkdLlkkcLnkDPskRpGsatakeil<-*
                      ++ +++ r+p+ ++++++  +Ll + +n  P+ Rp    + e++
  ratCARKpro   675 ADMAYHhiRPPIGYSIPKPISSLLIRGWNACPEGRP---EFSEVV    716
```

Fig. 6B

```
GAP of: AAAa006_n  check: 4956  from: 1  to: 3025

cark (analysis only) - Import - complete

to: BAAa006_n  check: 6389  from: 1  to: 3026

Rat CARK cDNA (analysis only) - Import - complete

Symbol comparison table: /ddm_local/gcg/gcg_9.1/gcgcore/data/rundata/
nwsgapdna.cmp
CompCheck: 8760

        Gap Weight:     12      Average Match: 10.000
     Length Weight:      4   Average Mismatch:  0.000

           Quality:  24376             Length:   3045
             Ratio:  8.058               Gaps:     14
Percent Similarity: 82.169   Percent Identity: 82.169

       Match display thresholds for the alignment(s):
                   | = IDENTITY
                   : =   5
                   . =   1

AAAa006_n x BAAa006_n
                .         .         .         .         .
     1 gtcgacccacgcgtccg.............gccctggagaaaggaagaaa 37  human
       |||||||||||||||||             || | ||||||| | | | |
     1 GTCGACCCACGCGTCCGGTGAAGGGCAGCAGCACAGGAGAAAAGCAAAGA 50  rat
                .         .         .         .         .
    38 cttataataaatgggaaattataaatctagaccaacccaaacttgtactg 87
       ||| |   |||||||| |||||| |||||| ||||||||| || ||||||| |||
    51 CTTCTTTAAAATGGGGAATTACAAATCCAGACCAACACAGACTTGTTCTG 100
                .         .         .         .         .
    88 atgaatggaagaaaaaagtcagtgaatcatatgttatcacaatagaaaga 137
       |||||||||||||| ||||| |||||||| || | ||| |  |||||||||
   101 ATGAATGGAAGAAGAAAGTTAGTGAATCTTACGCTATTATCATAGAAAGG 150
                .         .         .         .         .
   138 ttagaagatgacctgcagatcaaggaaaaagaactgacagaactaaggaa 187
        | || ||| |||||||||||||| ||||| ||| |   |||||||||| |
   151 CTGGAGGATAACCTGCAGATCAAAGAAAATGAATTTCAAGAACTAAGGCA 200
                .         .         .         .         .
   188 tatatttggctctgatgaagccttcagtaaagtcaatttaaattaccgca 237
        || |||||||||||||||||||||||| |||||| ||||||||||||||
   201 CATCTTTGGCTCTGATGAAGCCTTCAGTGAAGTCAGTTTAAATTACCGCA 250
                .         .         .         .         .
   238 ctgaaaatgggctgtctctacttcatttatgttgcatttgtggaggcaag 287
       | ||   ||| ||||| || || ||  | || ||  | ||||| ||||||
   251 CAGAGCGTGGCCTGTCCCTGCTACACCTCTGCTGTGTCTGTGGCGGCAAC 300
```

Fig. 7A

```
288 aaatcacatattcgaactcttatgttgaaagggctccgcccatctcgact 337
    || |||||||| ||  | ||||||||| |||||||||||| ||||||  ||||
301 AAGTCACATATCCGTGCCCTTATGTTAAAAGGGCTCCGTCCATCCAGACT 350

338 gacaagaaatggatttacagccttgcatttagcagtttacaaggataatg 387
    ||| |||||||| ||| |||| |||| | || |||||||||||| |
351 GACGAGAAATGGGTTTCCAGCTCTGCACCTGGCCGTTTACAAGGACAGCC 400

388 cagaattgatcacttctctgcttcacagtggagctgatatacagcaggtt 437
    | ||| | |||||||| ||| | ||||| ||||| ||| | ||||| ||
401 CGGAACTTATCACTTCACTGTTGCACAGCGGAGCAGATGTTCAGCAAGTG 450

438 ggatacggtggcctcactgccctccatattgctacaatagctggccacct 487
    |||||||||||||||||| |||||||| || ||| |||||||||| ||||
451 GGATACGGTGGCCTCACAGCCCTCCACATAGCTGCAATAGCTGGACACCC 500

488 agaggctgctgatgtgctgttgcaacatggagctaatgtcaatattcaag 537
    |||||||||| || ||||||| | ||||||||| || |||||| ||| |||||||
501 AGAGGCTGCAGAAGTGCTGCTACAACATGGGGCCAATGTGAATGTTCAAG 550

538 atgcagtttttttcactccattgcatattgcagcgtactatggacatgaa 587
    |||| || || |||||| ||| |||| ||||||||| ||||||||| || ||
551 ATGCCGTCTTCTTCACCCCACTGCACATTGCAGCCTACTATGGGCACGAG 600

588 caggtaactcgccttcttttgaaatttggtgctgatgtaaatgtaagtgg 637
    |||||||| | | ||||||||| |||||||||||||| ||||||||| ||
601 CAGGTAACCAGTGTCCTTTTGAAGTTTGGTGCTGATGTCAATGTAAGCGG 650

638 tgaagttggagatagacccctccacctagcatctgcaaaaggattcttga 687
    |||||||||| || || || || ||||| || ||||||||| || |||||  |
651 TGAAGTTGGGGACAGGCCTCTGCACCTGGCCTCTGCAAAGGGCTTCTTCA 700

688 atattgcaaaactcttgatggaagaaggcagcaaagcagatgtgaatgct 737
    | ||||  |||||| || | ||||||||| |||||||||||||||||| |||
701 ACATTGTGAAACTCCTGGTAGAAGAAGGGAGCAAAGCAGATGTGAACGCT 750

738 caagataatgaagaccatgtcccactccatttctgttctcgatttggaca 787
    || || |||||||||||| ||||| || || ||||||||||||||||||||
751 CAGGACAATGAAGACCACGTCCCTCTGCACTTCTGTTCTCGATTTGGACA 800

788 ccatgatatagttaagtatctgctgcaaagtgatttggaagttcaacctc 837
    |||  ||||||| |  || ||||| || ||||| || || || || |||||
801 CCACAATATAGTGAGCTACCTGCTCCAGAGTGACTTAGAGGTCCAGCCTC 850

838 atgttgttaatatctatggagatacccccttacacctggcatgctacaat 887
    | ||  |||| ||||||||| || || || || ||||||||||||||||||
851 ACGTCATTAACATCTATGGTGACACTCCTTTGCACCTGGCATGCTACAAT 900

888 ggcaaatttgaagttgccaaggaaatcatccaaatatcaggaacagaaag 937
    || || |||||||||||||||||||  ||||  || |||||||  ||||||
901 GGAAATTTTGAAGTTGCCAAGGAAATTGTCCAGGTAACAGGAACTGAAAG 950
```

Fig. 7B

```
 938 tctgactaaggaaaacatcttcagtgaaacagcttttcatagtgcttgta 987
     |||||||||||||||||||||||| || |||||||||||| ||||||||||
 951 TCTGACTAAGGAAAACATCTTCAGCGAGACAGCTTTTCACAGTGCTTGTA 1000

 988 cctatggcaagagcattgacctagtcaaatttcttcttgatcagaatgtc 1037
     |||||||||||| ||||||||| ||||||||||||||||||||||||||
1001 CCTATGGCAAGAACATTGACCTGGTCAAATTTCTTCTTGATCAGAATGCT 1050

1038 ataaacatcaaccaccaaggaagggatgggcacactggattacactctgc 1087
      | |||||| ||||||| |||||| |||||||||||| ||||| |||||||||
1051 GTGAACATTAACCACCGAGGAAGAGATGGGCACACAGGATTGCACTCTGC 1100

1088 ttgctaccacggtcacattcgcctggttcagttcttactggataatggag 1137
     |||||||||||| || || |||||||||||||||| |||| ||||||||| |
1101 TTGCTACCACGGCCATATCCGCCTGGTTCAGTTCCTACTTGATAATGGTG 1150

1138 ctgatatgaatctagtggcttgtgatcccagcaggtctagtggtgaaaaa 1187
     | |||||||||||| || ||||||||||||||||||||||||||||||||
1151 CAGATATGAATCTTGTCGCTTGTGATCCCAGCAGGTCTAGTGGTGAAAAA 1200

1188 gatgagcagacatgtttgatgtgggcttatgaaaaagggcatgatgccat 1237
     |||||||||||||||||||||||||||| || |||||| ||||||||||||
1201 GATGAGCAGACATGTTTGATGTGGGCTTACGAGAAAGGACATGATGCCAT 1250

1238 tgtcacactcctgaagcattataagagaccacaagatgaattgccctgta 1287
     ||| |||||||||||||| || |||||||| || || ||  |||| ||||
1251 TGTTACACTCCTGAAGCACTACAAGAGACCCCAGGAGGAGCTGCCATGTA 1300

1288 atgaatattctcagcctggaggagatggctcctatgtgtctgttccatca 1337
     | |||||||| ||||||||||||||||||||||||||||||||||| ||
1301 ACGAATATTCCCAGCCTGGAGGAGATGGCTCCTATGTGTCTGTTCCTTCC 1350

1338 cccttggggaagattaaaagcatgacaaaagagaaggcagatattctcct 1387
     |||||||| |||||||||||||||||||||||||||||||||| |||||||
1351 CCCTTGGGCAAGATTAAAAGCATGACAAAAGAGAAGGCAGATGTTCTCCT 1400

1388 cctaagagctggattgccttcacatttccatcttcagctctcagaaattg 1437
     ||| || |||| | | || || |  |||||||| || ||||| |||||| |
1401 CCTGAGGGCTGAACTACCCTCCCGCTTCCATCTCCAACTCTCCGAAATCG 1450

1438 agttccatgagattattggctcaggttcttttgggaaagtatataaagga 1487
     ||||||| ||||||||  ||||| ||||| |||||||||||  |||||||||
1451 AGTTCCACGAGATTATCGGCTCGGGTTCCTTTGGGAAAGTCTATAAAGGG 1500

1488 cgatgcagaaataaaatagtggctataaaacgttatcgagccaataccta 1537
     |||||||||||||||||||||||| || ||||| || |||||||| |||||
1501 CGATGCAGAAATAAAATAGTGGCGATCAAACGATACCGAGCCAACACCTA 1550
```

Fig. 7C

```
1538 ctgctccaagtcagatgtggatatgttttgccgagaggtgtccattctct 1587
     ||||||||||||||| ||||||||||||||||||||||||||||||||||||
1551 CTGCTCCAAGTCAGACGTGGATATGTTTTGCCGAGAGGTGTCCATTCTCT 1600

1588 gccagctcaatcatccctgcgtaattcagtttgtgggtgcttgcttgaat 1637
     |||||||||| || |||||||| |||||||||||||||| ||| || ||
1601 GCCAGCTCAACCACCCCTGCGTGGTTCAGTTTGTGGGTGCCTGCCTGGAT 1650

1638 gatcccagccagtttgccattgtcactcaatacatatcaggggttctct 1687
     || ||||| |||||||||||||||||||| ||||| ||||| || || ||
1651 GACCCCAGTCAGTTTGCCATTGTCACTCAGTACATTTCAGGAGGCTCCCT 1700

1688 gttctccctccttcatgagcagaagaggattcttgatttgcagtctaaat 1737
     ||||||||| |||||||| |||||||| |||||||| ||||||||||||
1701 GTTCTCCCTGCTTCATGAACAGAAGAGAATTCTTGACTTGCAGTCTAAAT 1750

1738 taattattgcagtagatgttgccaaaggcatggagtaccttcacaacctg 1787
     |||| ||||| ||||| |||||||| |||||||||||||| |||| | ||
1751 TAATCATTGCGGTAGACGTTGCCAAGGGCATGGAGTACCTGCACAGCTTG 1800

1788 acacagccaattatacatcgtgacttgaacagtcacaatattcttctcta 1837
     || |||||||| ||||| || ||| ||||||| |||||||||||| |||||
1801 ACCCAGCCAATCATACACCGCGACCTGAACAGCCACAATATTCTGCTCTA 1850

1838 tgaggatgggcatgctgtggtggcagattttggagaatcaagatttctac 1887
     ||||||||| |||||||||||||||||||||||||||||||||||||| |
1851 TGAGGATGGCCATGCTGTGGTGGCAGATTTTGGAGAATCAAGATTTCTGC 1900

1888 agtctctggatgaagacaacatgacaaaacaacctgggaacctccgttgg 1937
     |||| |||||||||||||||||||| || || |||||||| || |||
1901 AGTCCCTGGATGAAGACAACATGACAAAGCAGCCAGGGAACCTGCGCTGG 1950

1938 atggctcctgaggtgttcacgcagtgcactcggtacaccatcaaagcaga 1987
     ||||| |||||||||||||| |||||||| | |||||||||| || ||
1951 ATGGCCCCTGAGGTGTTCACACAGTGCACGAGATACACCATCAAGGCTGA 2000

1988 tgtcttcagctatgctctgtgtctgtgggaaattctcactggcgaaattc 2037
     ||||||||| ||  | |||||||||||||  | |||||||| |||||||
2001 TGTCTTCAGTTACTCCCTGTGTCTGTGGGAGCTCCTCACTGGAGAAATTC 2050

2038 cattcgctcatctcaagccagcggctgcggcagcagacatggcttaccac 2087
     |||||||||||||||||||||| ||||| |||||||| ||||| || |||
2051 CATTCGCTCATCTCAAGCCAGCCGCTGCAGCAGCAGATATGGCGTATCAC 2100

2088 cacatcagacctcccattggctattccattcccaagcccatatcatctct 2137
     |||||||||||| ||||| |||||||||||| |||||||||| ||||| ||
2101 CACATCAGACCGCCCATCGGCTATTCCATCCCCAAGCCCATCTCATCCCT 2150

2138 gctgatacgagggtggaacgcatgtcctgaaggaagacccgaattttctg 2187
     ||||||||| || |||||| |||||||||||||||| |||| || || ||||
2151 GCTGATACGGGGCTGGAATGCATGTCCTGAAGGACGACCAGAGTTCTCTG 2200
```

Fig. 7D

```
2188 aagttgtcatgaagttagaagagtgtctctgcaacattgagctgatgtct 2237
     |||| || |  ||  | || ||||| || |||||  | |||||  |||||| 
2201 AAGTCGTTAGCAAACTGGAGGAGTGCCTATGCAATGTGGAGCTCATGTCT 2250

2238 cctgcatcaagtaacagcagtgggtctctctcaccttcttcttcttctga 2287
     || |||||||||||||||||||| ||||| |||||||| |||||||| || 
2251 CCAGCATCAAGTAACAGCAGTGGCTCTCTGTCACCTTCCTCTTCTTCCGA 2300

2288 ttgcctggtgaaccggggaggacctggccggagtcatgtggcagcattaa 2337
     ||||||| ||| |||||||||| |||||||||||  || |||||||| ||| 
2301 TTGCCTGCTGAGCCGGGGAGGGCCTGGCCGGAGCCACGTGGCAGCCTTAC 2350

2338 gaagtcgtttcgaattggaatatgctctaaatgcaaggtcctatgctgct 2387
     | || ||||| || ||||| ||||| |||||||||||||||||||||| 
2351 GGAGCCGTTTTGAGTTGGAGTATGCCCTAAATGCAAGGTCCTATGCTGGG 2400

2388 ttgtcccaaagtgctggacaatattcctctcaaggtctgtctttggagga 2437
     | |||||||||||| ||||  | |  ||   ||  || ||||||||||||| 
2401 TGGTCCCAAAGTGTTGGAACACACTCTAATCCGGGCCTGTCTTTGGAGGA 2450

2438 gatgaaaagaagtcttcaatacacacccattgacaaatatggctatgtat 2487
     ||||||  ||  ||    ||  ||  ||  |  |||||||||| |||||||| | 
2451 GATGAATAGGAGCACCCAGTATTCAACTGTTGACAAATACGGCTATGTGT 2500

2488 ccgatcccatgagctcaatgcattttcattcttgccgaaatagtagcagc 2537
     | ||||||||||||    | |||  ||||  ||  |||  | |    ||||  | 
2501 CTGATCCCATGAGCCTGACGCACCTTCACTCCCGCCAAGACGACAGCAAC 2550

2538 tttgaggacagcagctgacagcattcggcgtatacctaaggagagttttt 2587
     |||||||||||||| |||||||  |  |||  ||  |||||||| | ||  | 
2551 TTTGAGGACAGCAACTGACAG.GTCTGGCATACACCTAAGGGGCGTCTCC 2599

2588 tccccgaactgacagcaacgattccaaccacggcaagctggcttccaact 2637
      |  |  |||||||||  ||||  | |||  ||||  |||  |||||||| | 
2600 CCATCAGGCTGACAGCAGTGATTTTACCCATGGCAGGCTTGCTTCCAATT 2649

2638 ataacattttactctcaaaggtctccttaaattgggcttgtttttacttg 2687
     |||||    | |  |||  ||||  | |||  ||  | |  ||||  ||  |  || 
2650 ATAACGCCCTGCCCTCTGAGGT.TTCTTCAAATCGTCTTGCTTATTCTAA 2698

2688 tcctatttaattccccactattag.caggctttggatttgtgcctaagga 2736
      |  ||||||||||  |||  | |||||||| ||  |  ||||  | | 
2699 GCTCGTTTAATTCCCTTCTACAGGACAGGCTTT.GACTCATGCC..AAGC 2745

2737 ataatatgcaaaagaaccaagacagaatgtatatgaagaattgtttttaa 2786
      | |  ||  |||||  |  | ||||||||||  ||||  |||||||| |||
2746 CTGAAGTGTCAAAGAGCAGATACAGAATGTGCATGAGGAATTGTTCTTAG 2795
```

Fig. 7E


2787 ttttgtaaattaaaaaaaaatttagatcgttacttggaaatggagcctaa 2836
2796 TTTGATATTT....AAAGCCCTTA....ATTGCCTGGGGCTGGGGTTCAA 2837
2837 gtctgtggtggaca.....gataataattatgttttcctgggctgaatta 2881
2838 ATCTGT.GTAGATAGCTGGGTTGACCCTTATGTATTTGTAGACCAAACTG 2886
2882 tgtagacttgtgtttgacag.ctatgggtttatttcttagaacattgttc 2930
2887 TGTGGGCTTGTGTTTGAGGGTCTCCTGTTGGGTTTCTTAAAAACAAGCTG 2936
2931 attttcttttctcattatgttacttctagtgttcacctctgtgattaaag 2980
2937 GCTGATTTATCTC...CTGTTGCCTTTGTTGTT.ACTTCTGTGATTAAAG 2982
2981 attctttggtgaaatagaaaaaaaaaaaaaaaaaagggcggccgc 3025
2983 TCTCTTCGGTGATCTAG.AAAAAAAAAAAAAAAAAGGGCGGCCGC 3026

Fig. 7F

```
GAP of: IAAa006_n  check: 1490  from: 1  to: 836

ratCARKpro (analysis only) - Import - complete

to: JAAa006_n  check: 4709  from: 1  to: 835

carkprot (analysis only) - Import - complete

Symbol comparison table: /prod/ddm/seqanal/B:AST/matrix/aa/BLOSUM62
CompCheck: 1102
 Matrix made by matblas from blosum62.iij

        Gap Weight:     12      Average Match:  2.778
     Length Weight:      4   Average Mismatch: -2.248

           Quality:   4079             Length:    836
             Ratio:  4.885               Gaps:      0
Percent Similarity: 93.174   Percent Identity: 91.377

       Match display thresholds for the alignment(s):
                   | = IDENTITY
                   : =   2
                   . =   1

IAAaoo6_n x JAAa006_n

                .         .         .         .         .
  1 MGNYKSRPTQTCSDEWKKKVSESYAIIIERLEDNLQIKENEFQELRHIFG 50   rat
    |||||||||||||.|||||||||||| | ||||||.||||| |  |||.|||
  1 MGNYKSRPTQTCTDEWKKKVSESYVITIERLEDDLQIKEKELTELRNIFG 50   human
                .         .         .         .         .
 51 SDEAFSEVSLNYRTERGLSLLHLCCVCGGNKSHIRALMLKGLRPSRLTRN 100
    ||||||.|.|||||| ||||||||||:||| ||||| ||||||||||||||
 51 SDEAFSKVNLNYRTENGLSLLHLCCICGGKKSHIRTLMLKGLRPSRLTRN 100
                .         .         .         .         .
101 GFPALHLAVYKDSPELITSLLHSGADVQQVGYGGLTALHIAAIAGHPEAA 150
    || |||||||||. ||||||||||||:|||||||||||||| |||| |||
101 GFTALHLAVYKDNAELITSLLHSGADIQQVGYGGLTALHIATIAGHLEAA 150
                .         .         .         .         .
151 EVLLQHGANVNVQDAVFFTPLHIAAYYGHEQVTSVLLKFGADVNVSGEVG 200
    :||||||||||:|||||||||||||||||||| .|||||||||||||||
151 DVLLQHGANVNIQDAVFFTPLHIAAYYGHEQVTRLLLKFGADVNVSGEVG 200
                .         .         .         .         .
201 DRPLHLASAKGFFNIVKLLVEEGSKADVNAQDNEDHVPLHFCSRFGHHNI 250
    |||||||||||| || |||.||||||||||||||||||||||||||||||
201 DRPLHLASAKGFLNIAKLLMEEGSKADVNAQDNEDHVPLHFCSRFGHHDI 250
                .         .         .         .         .
251 VSYLLQSDLEVQPHVINIYGDTPLHLACYNGNFEVAKEIVQVTGTESLTK 300
    | |||||||||||||:|||||||||||||| |||||||:|:.|||||||
251 VKYLLQSDLEVQPHVVNIYGDTPLHLACYNGKFEVAKEIIQISGTESLTK 300
```

Fig. 8A

```
301 ENIFSETAFHSACTYGKNIDLVKFLLDQNAVNINHRGRDGHTGLHSACYH 350
    |||||||||||||||||.|||||||||||| :||||.|||||||||||||||
301 ENIFSETAFHSACTYGKSIDLVKFLLDQNVININHQGRDGHTGLHSACYH 350

351 GHIRLVQFLLDNGADMNLVACDPSRSSGEKDEQTCLMWAYEKGHDAIVTL 400
    ||||||||||||||||||||||||||||||||||||||||||||||||||
351 GHIRLVQFLLDNGADMNLVACDPSRSSGEKDEQTCLMWAYEKGHDAIVTL 400

401 LKHYKRPQEELPCNEYSQPGGDGSYVSVPSPLGKIKSMTKEKADVLLLRA 450
    ||||||||:||||||||||||||||||||||||||||||||||:||||||
401 LKHYKRPQDELPCNEYSQPGGDGSYVSVPSPLGKIKSMTKEKADILLLRA 450

451 ELPSRFHLQLSEIEFHEIIGSGSFGKVYKGRCRNKIVAIKRYRANTYCSK 500
     ||| ||||||||||||||||||||||||||||||||||||||||||||||
451 GLPSHFHLQLSEIEFHEIIGSGSFGKVYKGRCRNKIVAIKRYRANTYCSK 500

501 SDVDMFCREVSILCQLNHPCVVQFVGACLDDPSQFAIVTQYISGGSLFSL 550
    ||||||||||||||||||||||:||||||||.||||||||||||||||||
501 SDVDMFCREVSILCQLNHPCVIQFVGACLNDPSQFAIVTQYISGGSLFSL 550

551 LHEQKRILDLQSKLIIAVDVAKGMEYLHSLTQPIIHRDLNSHNILLYEDG 600
    ||||||||||||||||||||||||||||.||||||||||||||||||||
551 LHEQKRILDLQSKLIIAVDVAKGMEYLHNLTQPIIHRDLNSHNILLYEDG 600

601 HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFS 650
    ||||||||||||||||||||||||||||||||||||||||||||||||||
601 HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFS 650

651 YSLCLWELLTGEIPFAHLKPAAAAADMAYHHIRPPIGYSIPKPISSLLIR 700
    |.||||||:||||||||||||||||||||||||||||||||||||||||||
651 YALCLWEILTGEIPFAHLKPAAAAADMAYHHIRPPIGYSIPKPISSLLIR 700

701 GWNACPEGRPEFSEVVSKLEECLCNVELMSPASSNSSGSLSPSSSSDCLL 750
    |||||||||||||||| ||||||||:||||||||||||||||||||||.
701 GWNACPEGRPEFSEVVMKLEECLCNIELMSPASSNSSGSLSPSSSSDCLV 750

751 SRGGPGRSHVAALRSRFELEYALNARSYAGWSQSVGTHSNPGLSLEEMNR 800
    .|||||||||||||||||||||||||||||  ||| | :|. |||||||||
751 NRGGPGRSHVAALRSRFELEYALNARSYAALSQSAGQYSSQGLSLEEMKR 800

801 STQYSTVDKYGYVSDPMSLTHLHSRQDDSNFEDSNX 836
    | ||. :||||||||||||  | || .. |.||||.
801 SLQYTPIDKYGYVSDPMSSMHFHSCRNSSSFEDSS. 835
```

Fig. 8B

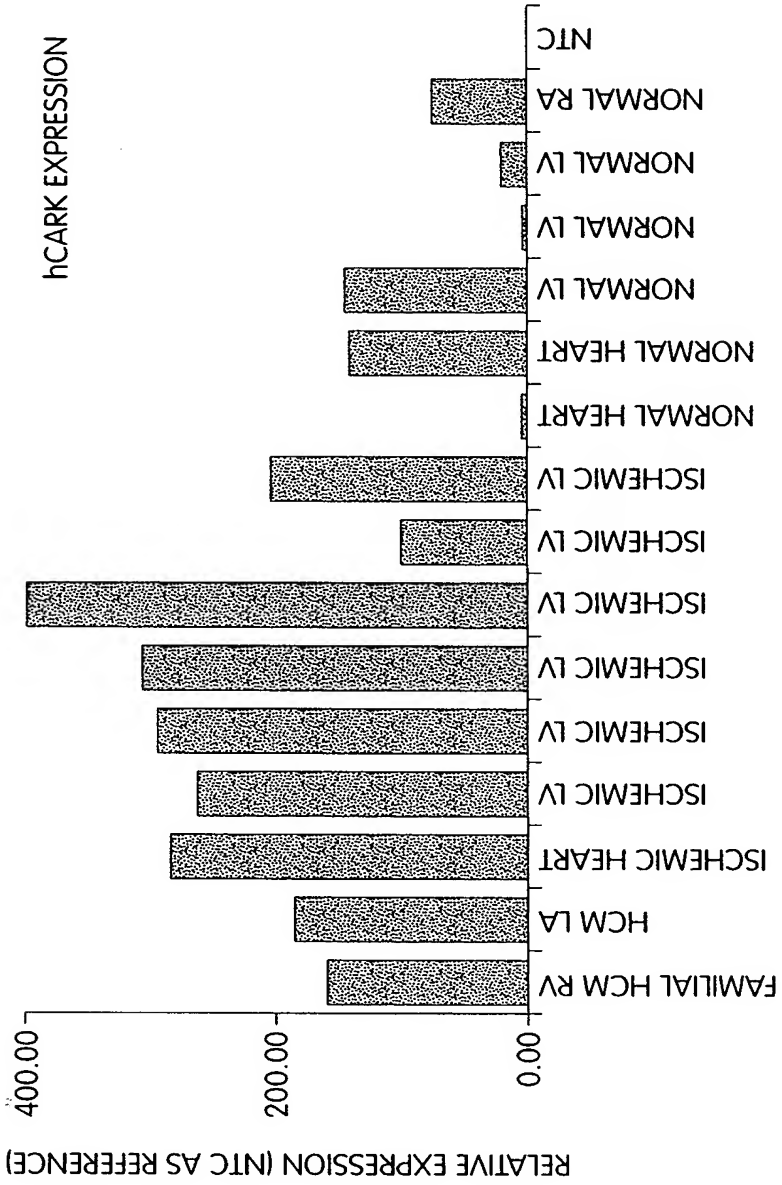
hCARK EXPRESSION
NTC
NORMAL RA
NORMAL LV
NORMAL LV
NORMAL LV
NORMAL HEART
NORMAL HEART
ISCHEMIC LV
ISCHEMIC LV
ISCHEMIC LV
ISCHEMIC LV
ISCHEMIC LV
ISCHEMIC LV
ISCHEMIC HEART
HCM LA
FAMILIAL HCM RV
400.00
200.00
0.00
RELATIVE EXPRESSION (NTC AS REFERENCE)

Fig. 9

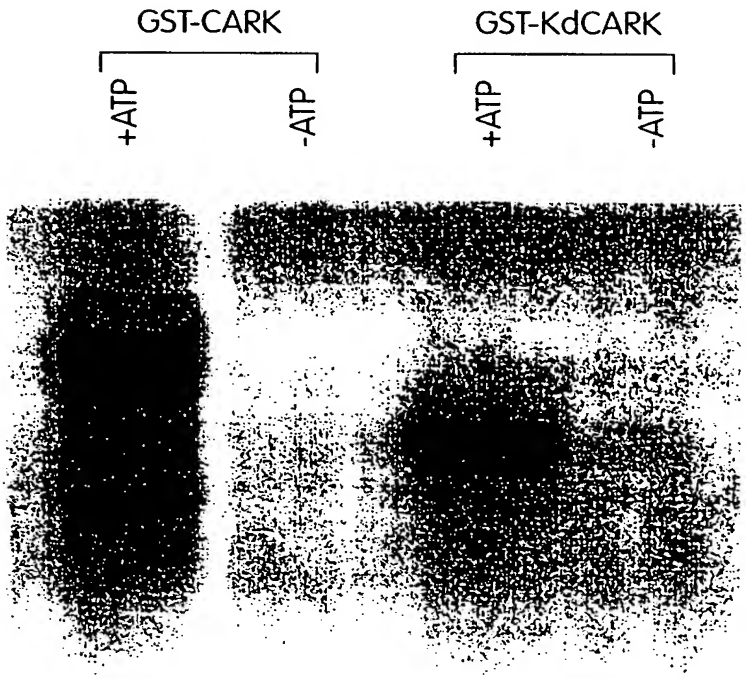

Fig. 10

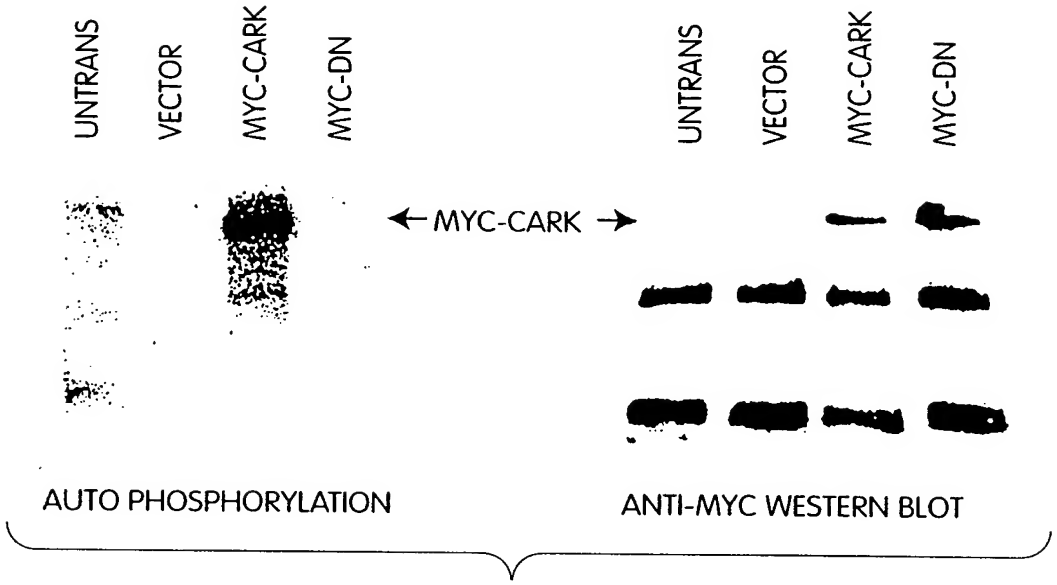
UNTRANS
VECTOR
MYC-CARK
MYC-DN
UNTRANS
VECTOR
MYC-CARK
MYC-DN
← MYC-CARK →
AUTO PHOSPHORYLATION
ANTI-MYC WESTERN BLOT

Fig. 11

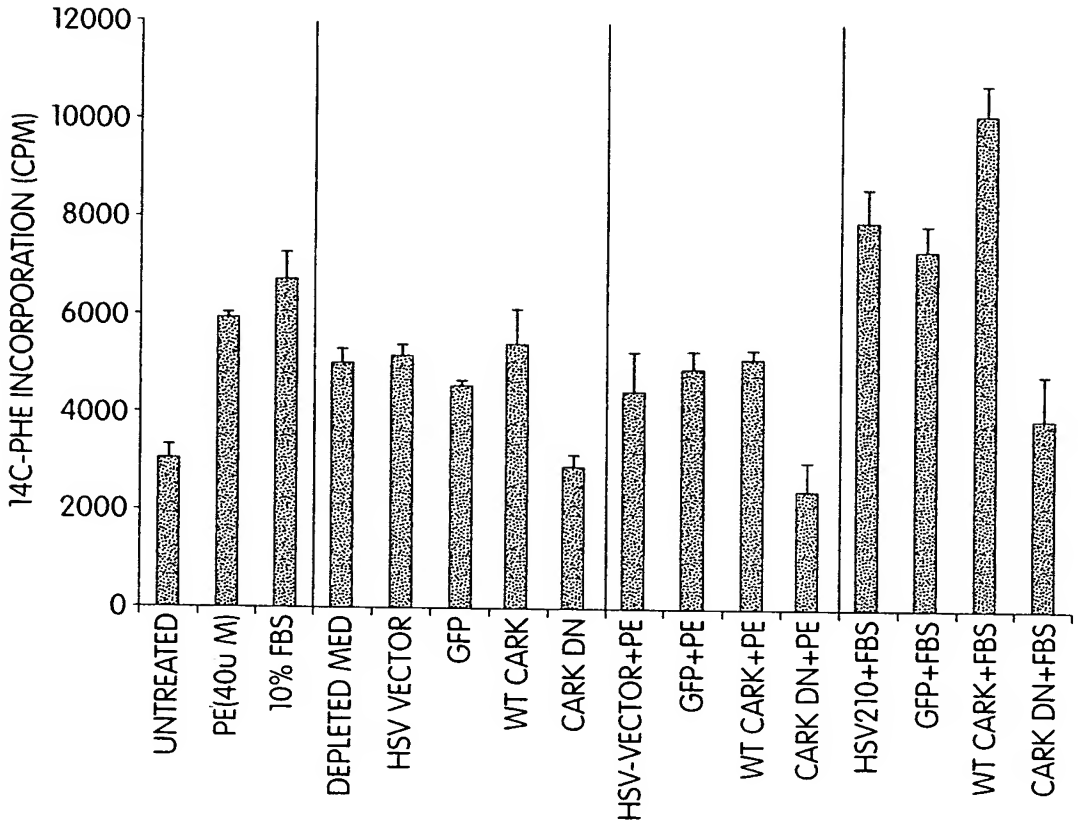
14C-PHE INCORPORATION (CPM)
12000
10000
8000
6000
4000
2000
0
UNTREATED
PE(40u M)
10% FBS
DEPLETED MED
HSV VECTOR
GFP
WT CARK
CARK DN
HSV-VECTOR+PE
GFP+PE
WT CARK+PE
CARK DN+PE
HSV210+FBS
GFP+FBS
WT CARK+FBS
CARK DN+FBS

Fig. 12